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PRINCIPAL INVESTIGATOR: Dr. Grace Smith

CONTRACTING ORGANIZATION: University of Texas M.D. Anderson Cancer Center
Houston, TX 77030

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Dr. Grace Smith

E-Mail: tbuchhol@mdanderson.org

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14. ABSTRACT

Scope and Purpose. Prior research evidence that has suggested that regional variation and socioeconomic barriers in breast cancer treatment remain substantial problems for patients across the nation. The purpose of our project was to characterize national patterns in the treatment of early invasive breast cancer in older women with incident disease. Methods. We sought to apply a novel resource, comprehensive national Medicare claims data, to study variations in treatment, cost of care, and outcomes in women treated for breast cancer. We first identified patients with invasive breast cancer treated with mastectomy or breast conserving surgery (BCS) and evaluated variations by geographic location, and also other covariates such as race. Multivariate logistic and linear regression was used to model outcomes. Findings. Significant regional variation in utilization of breast cancer treatment existed in our cohort of older women diagnosed with invasive disease, even after standardization for patient and disease characteristics. In addition, significant disparities in costs or spending for breast cancer existed, with not only patient and clinical factors playing a significant role in costs, but also socioeconomic factors. Finally, significant variation, particularly geographic variation, was found in patient outcomes including survival. Conclusions. Our research adds to the existing literature by providing the first comprehensive national sample to address these study questions. Our future research will extend on our current findings by determining whether these variations may have changed over time and whether newer technologies have been affected by similar utilization patterns.

15. SUBJECT TERMS

Breast cancer, Medicare, utilization, breast-conserving surgery, mastectomy

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INTRODUCTION

The purpose of our project was to characterize national patterns in the treatment of early invasive breast cancer in older women with incident disease. We specifically sought to characterize disparities in care and regional variation in treatment patterns. Our study subject was in response to prior research evidence that has suggested that regional variation and socioeconomic barriers in breast cancer treatment remain substantial problems for patients across the nation. In fact, though a full decade ago, in 1999, the Institute of Medicine National Cancer Policy Board issued a call to improve the quality of cancer care nationally[1], still recent data indicate that progress in overcoming disparities in cancer care has been insufficient[2]. For our project, we applied a novel resource, comprehensive national Medicare claims data, to study disparities in care and outcomes in women with breast cancer. Our project has spanned a total of three years.

At the culmination of Year 1 of this project, our main objective was to characterize the scope of treatment disparities and the magnitude of regional variation in care, using cross-sectional data. At the culmination of Year 2, we assessed the factors that impacted the choices for treatment—including non-standard and developing treatment—as well as the implications of these treatment choices on variations on spending (cost) in breast cancer care. At the culmination of Year 3, we assessed the impact of utilization patterns on breast cancer outcomes. The following narrative will summarize results obtained over Years 1 through 3.

BODY

Task Summary from Statement of Work (SOW)

Task 1. To assess standardized utilization rates of radiation therapy and chemotherapy.
Objectives
Analysis 1: To present overall national and state-by-state absolute and standardized utilization rates of treatment
Analysis 2: To present utilization rates of radiotherapy (RT) after conservative surgery (CS) by race, a significant modifying factor, in order to quantify disparities in breast cancer treatment, given that RT after CS is generally considered standard therapy
Analysis 3: To present utilization rates of brachytherapy, in order to help quantify the uptake in an emerging area of treatment across the United States
Analysis 4: To present a validation sample of breast cancer patients and evaluate and validate the utility of claims-based covariates in predicting breast cancer stage
*Please also see **Annual Report, September 2008**.

Task 2. To assess initial and continuing care costs of breast cancer care.
Objectives
Analysis 1: To present overall national and state-by-state absolute and standardized utilization rates of mastectomy versus breast-conserving surgery (BCS)
Analysis 2: To identify variations and disparities in use of mastectomy versus BCS

Analysis 3: To quantify the costs associated with mastectomy and BCS, and to compare these costs with other breast cancer treatment related spending, including chemotherapy, radiotherapy, and other surgeries
Analysis 4: To compare breast cancer associated costs with non cancer associated costs in the year after cancer diagnosis
Analysis 5: To identify predictors of breast cancer-related costs, including treatment, disease, patient, and socioeconomic factors
Analysis 6: To present utilization rates of brachytherapy, an emerging but potentially costly breast cancer treatment, in order to help quantify the diffusion of this technology in an emerging area of treatment across the United States and discuss the implications of findings on the future incorporation of costly treatments and technologies.
*Please also see **Annual Report, September 2009**.

Task 3. To assess outcomes relevant to breast cancer.
Objectives
Analysis 1: To create a longitudinal cohort of breast cancer patients treated with BCS, with or without RT.
Analysis 2: To examine overall survival rates in patients treated with vs. without RT.
Analysis 3: To examine geographic variation in survival.

Methods

Study sample

Our main study sample of patients diagnosed with invasive breast cancer and treated with either BCS or mastectomy was derived from the national Medicare dataset. In addition, we used several subsamples in our analysis to accomplish the above mentioned objectives, which will also be detailed below.

Medicare. The national Medicare dataset includes comprehensive claims information with beneficiary-specific data on all Medicare beneficiaries in the United States. Files contain data collected by Medicare for reimbursement of health care services for each beneficiary and include institutional (inpatient and outpatient) as well as non-institutional (physician or other providers) final action claims[3].

Cross-sectional cohort. To define a cohort of patients with incident disease in 2003 required claims data spanning 2002 to 2004 to have complete information on the claims history the year prior to diagnosis and information on claims up a year after diagnosis, as detailed below. In summary, our initial study population consisted of 853,273 women who had any diagnosis of invasive breast cancer in 2003, based on an International Classification of Diseases, Ninth Revision (ICD-9) diagnosis code of 174. As this denominator would have included incident and prevalent cases in 2003, we used the following algorithm to identify patients with incident breast cancer, treated with either breast-conserving surgery (BCS) or mastectomy. This method was based on a prior validated algorithm for claims data.[4, 5] We included women (age≥65 years)

who had any diagnosis of invasive breast cancer in 2003 (defined as an International Classification of Diseases, Ninth Revision (ICD-9) diagnosis code of 174) who underwent BCS (N= 83,611) or mastectomy (N=42,504) between January 1, 2003, and December 31, 2003. From this sample, to increase the specificity of the definition, we excluded 23,715 patients who did not have at least 2 claims (on different dates) indicating a diagnosis of invasive breast cancer between January 1, 2003 and December 31, 2004 (at least 1 claim must have occurred during 2003), with no more than 6 months between the date of BCS or mastectomy and the earliest breast cancer diagnosis claim date. To exclude the prevalent cases, we excluded 16,471 patients who had a breast cancer–related diagnosis or procedure claim between January 1, 2002, and December 31, 2002. To reduce misclassification of the primary intended surgery, we excluded 630 patients who underwent both types of surgery (either date of mastectomy claim preceding date of BCS claim or mastectomy occurring more than 3 months after BCS), except for patients who received a mastectomy within 3 months of BCS for whom mastectomy was considered the definitive surgery. To limit our sample to patients with non-metastatic invasive breast cancer, we then excluded 2,122 patients who had two or more claims specifying metastatic breast cancer from 3 months before to 3 months after the diagnosis date. To improve sample homogeneity, we also excluded 5,719 patients who were receiving Medicare coverage because of end-stage renal disease or disability. Finally, to ensure we had complete claims information to determine patients' cancer treatment course and comorbidities, we excluded 6,612 patients who lacked Part A or B coverage or who had intermittent health maintenance organization coverage in the 9 months after or in the 1 year before their breast cancer diagnosis date (of these patients, 3,561 had incomplete information in the year prior to diagnosis because they were <66 years of age). For this analysis, the breast cancer diagnosis date was defined as the date of the earliest claim for a diagnosis of breast cancer. This left a final sample size of 56,725 patients. Our algorithm was based on a prior validated algorithm for identifying breast cancer patients using claims data[4].

Longitudinal cohort. We subsequently derived a longitudinal cohort, which included breast cancer patients (as defined by the algorithm above) diagnosed between 2000 and 2003. In addition, we retained all denominator and claims data for these patients through 2004, thus allowing for up to four-year follow-up in these patients.

Surgical treatment and other covariates

Covariates derived from Medicare files (denominator and claims files) included cancer treatment variables, other clinical variables, and demographic data. Patients were classified as treated with BCS or mastectomy if a claim for the surgery (Appendix A) occurred within 6 months of the breast cancer diagnosis date. Claims for chemotherapy must have occurred within 6 months and RT claims within 9 months of the breast cancer diagnosis date. These claims-based treatment definitions have been applied in prior studies of breast cancer patients.[6-11]

Other disease- and treatment-related variables included axillary lymph node involvement, axillary lymph node dissection, sentinel node biopsy, receipt of any RT (including brachytherapy), receipt of any chemotherapy, specific receipt of doxorubicin or paclitaxel,

receipt of any imaging studies for staging, number of hospitalizations in the year after diagnosis, and number of medical oncology, radiation oncology, and surgery visits in the year after diagnosis. Of patients who received RT, patients were further classified as having received external beam radiation therapy (EBRT), brachytherapy, or both (EBRT plus brachytherapy boost), as indicated by claims codes. Patients treated with brachytherapy were further classified as having received balloon-based treatment if a procedure code was found specifying accordingly.

Variables indicating preventive healthcare and interactions with the healthcare system included mammography in the year prior to diagnosis and number of physician visits in the year prior to diagnosis. In addition, we calculated the severity of comorbid disease for each patient based on a modified Charlson comorbidity score validated in a prior claims-based study: 0 (no comorbidity), 1 (mild to moderate), or 2 or more (severe)[12]. This score combined comorbidities recorded in Medicare claims during the 12 months prior to the patient's cancer diagnosis. To enhance specificity of comorbid disease diagnoses, patients must have had at least 1 inpatient (Part A) claim or at least 2 outpatient (Part B) claims more than 30 days apart.[12]

Demographic data available through Medicare files included patient age at diagnosis, race (categorized as white, black, and other), and state and county of residence. Classification of geographic regions was based on Census Divisions definitions.[13] Socioeconomic variables, obtained from the 2003 Area Resource File (ARF)[14] and linked to the Medicare dataset by patients' county, included (by county of patient's residence) median household income, percent living below poverty level, percent completing ninth grade education, high school, and college. Supply of healthcare providers (for breast cancer treatment) was measured by the density of general surgeons, and density of radiation oncologists at county-level, obtained from the 2003 ARF.

Predictor covariates were obtained by searching through inpatient, outpatient, and carrier Medicare claims or the denominator file for SEER-Medicare linked data for demographic variables. A comprehensive list of International Classification of Diseases, Ninth Revision (ICD-9), Common Procedural Terminology (CPT), and Revenue Center codes for each predictor are listed in **Table 1**.

Cost

Total health care costs for each patient were calculated based on Medicare spending. Any claim, and the associated total payment amount reported by Medicare, identified through the inpatient, outpatient, or carrier claims files was added, for a sum total of costs in the year after breast cancer diagnosis. Breast-cancer related spending was summed for each patient with claims belonging in the following categories: surgery (mastectomy, BCS, or reconstruction after mastectomy), axillary nodal dissection or involvement, chemotherapy, radiotherapy, and other breast cancer diagnosis-related claim.

Survival

All-cause mortality is tracked through Medicare claims, specifically through the denominator data. Thus we searched longitudinal claims to obtain a date of death. If date of death was missing, then the patient was assumed to be alive at last follow-up.

Statistical analyses

Statistical analyses were conducted using SAS version 9.1.3 (SAS Institute Inc, Cary, NC), and all statistical tests assumed a 2-tailed α of 0.05.

Treatment utilization. (See details in **Annual Report, September 2008 and Annual Report, September 2009**) For characterization of treatment utilization, bivariate associations between treatment (radiotherapy and chemotherapy; percent BCS versus mastectomy) and other covariates were tested using the Pearson chi-square test for categorical variables and the Wilcoxon rank sum test for continuous variables. Percent BCS versus mastectomy use was calculated for the entire sample, by state, and by region. A multivariate logistic model tested the adjusted association between predictors and treatment. Covariates were selected *a priori* based on significance in bivariate analyses (P<0.25) and significance in prior studies of cancer patients[6-12]. Logistic models also derived standardized treatment rates, based on unadjusted percent use of radiotherapy and chemotherapy, standardized for covariates.

Outcomes. (See details in **Annual Report, September 2009**) Mean breast cancer-related and overall healthcare costs were calculated for the entire sample, by state, and by region. A multivariate logistic model tested adjusted associations with BCS and a multivariate linear regression model tested adjusted associations with breast cancer-related costs, with covariates for the final multivariate models selected *a priori* based on significance in bivariate analyses (*P<0.25*) and significance in prior studies of cancer patients[19-24] The final parsimonious model was selected based on statistical significance, goodness of fit, and minimizing multicollinearity. Finally, percent died over longitudinal follow-up was calculated for the entire sample, by state, and by region.

Early stage breast cancer subgroup

Breast cancer stage is not directly available through Medicare claims data. To select a subgroup of patients with early stage breast cancer, given that surgical treatment strategies are typically dependent on disease stage, we applied a previously validated predictive algorithm that used claims-based covariates to identify patients with a high probability of having stage I or II disease.[15] (See also, **Annual Report, September 2008**). Therefore, in the selected subgroup of 43,706 predicted early stage patients, we further examined the adjusted associations between receipt of BCS and covariates using multivariate logistic modeling.

In a secondary, validating analysis on this selected group of predicted early stage patients, we also identified the subgroup of 42,499 patients who did not have claims for axillary involvement and chemotherapy, as these patients would also be more likely to have early stage disease (kappa=0.73 for the two selected subgroups). The adjusted associations were compared in this group to the associations calculated for the predicted early stage patients.

Brachytherapy pilot subgroup

(See also, **Annual Report, September 2009)** A limitation of the current national Medicare data-based cohort for our analysis is that, for the study of treatment patterns, this is essentially a cross-sectional sample (as the initial course of cancer treatment can occur months

or even up to a year after the date of diagnosis). Thus, for the study of temporal patterns, the national Medicare data is particularly limited. Therefore, we sought to study a pilot sample derived from the The MarketScan® Medicare Supplemental database is a large, nationwide, employment-based claims database which includes Medicare beneficiaries with private supplemental insurance obtained through their former employers. We identified 6,882 women aged 65 years and older with a diagnosis of invasive breast cancer and treated with BCS. Using the same algorithm as listed above, patients who had claims for RT were further classified as having received as treated with external beam radiation therapy (EBRT), brachytherapy, or both (EBRT plus brachytherapy boost), as indicated by claims codes. Patients treated with brachytherapy were further classified as having received balloon-based treatment if a procedure code was found specifying accordingly. To address our second objective, we evaluated for a time trend using the Mantel-Hanszel chi-square and Cochran-Armitage tests for trend. We also benchmarked the time trends against two major policy events that occurred during the study period: Food and Drug Administration (FDA) approval of the first balloon-based brachytherapy device for breast cancer in June 2002; and Medicare reimbursement of breast brachytherapy in April 2004.

Table 1. Claims codes searched to calculate costs and define variables of interest

Variables	ICD-9 Diagnosis	ICD-9 Procedure	CPT	Revenue Center
Radiotherapy				
EBRT		9221-6, 9228, 9229	77427, 77431-2, 77401-9, 77411-14, 77416, 77418, 77470, 77499, 77520, 77522-3, 77525, 77750, 77789, 77790	0330, 0333
Brachytherapy		9227	19296-8, 77326-8, 77761-3, 77776-8, 77781-4, Q3001, C9714-5	
Balloon-based brachytherapy			C9714-5	
Extent of disease at diagnosis				
Axillary LN involvement	1963			
Metastatic disease	1962, 1965-6, 197, 1970, 1971, 1972, 1973, 1974, 1975, 1976, 1977, 1978, 198, 1980, 1981, 1982, 1983, 1984, 1985, 1986, 1987, 1988, 19881, 19882, 19889			

Table 1, *continued*

Variables	ICD-9 Diagnosis	ICD-9 Procedure	CPT	Revenue Center
Cancer diagnosis and treatment				
Imaging (CT, MRI, PET, or bone scan)		8801, 8703, 8741, 8891, 8896, 8874, 9218, 9214	70450, 70460, 70470, 70551-3, 71250, 71260, 71270, 72192-4, 74150, 74160, 74170, 76700, 78315, 78320, 78812-6, G0213-5	
Breast conserving surgery		8520-3,8525	19110, 19120, 19125, 19160, 19162	
Mastectomy		8541-8	19180, 19182, 19200, 19220, 19240	
Axillary surgery (LN dissection or sentinel node)		4023, 4051, 8543, 8547	38500, 38525, 38740, 38745, 38792, 19162, 19200, 19220, 19240, 78195	
Chemotherapy (any agent)	V581, V662, V672	9925	96400-96549, J9000-9, Q0083-5	0331, 0332, 0335
Preventive care and interaction with healthcare system				
No. physician visits				
Screening mammography	V7611, V7612	8737, 8736	77055-6, 77058-9, 76090-2, G0202, G0204, G0206	0401, 0403
Influenza vaccine	V0481		90658, G0008	
General health status				
Charlson comorbidity score[a]				

Abbreviations: CPT Common Procedural Terminology; ICD International Classification of Diseases; LN lymph node; No. number.

[a] Klabunde CN, et al. J Clin Epidemiol 2000;53:1258-1267.

Results

Patient characteristics and treatment course

Our cohort consisted of 56,725 women with incident, invasive breast cancer diagnosed in 2003 and treated with surgery. In our sample, median age was 76 (interquartile range 71 to 81). Ninety percent (N=51,432) were white, 7% (N=3,727) were black, and 3% (N=1,566) were of other race. As a component of the initial treatment course, the majority of patients were treated with BCS. Specifically, 59% of patients (N=33,450) received BCS, while 41% (N=23,275) underwent mastectomy. Additionally, of the entire sample, 50% received RT and 16% received chemotherapy. Of BCS patients, 74% received RT and 13% received chemotherapy. Of mastectomy patients, 14% received RT and 23% chemotherapy.

Part I: (for further details, please see **Annual Report, September 2008)**.
Predictors of chemotherapy and RT
Utilization of RT and chemotherapy across the United States

Absolute percent use and standardized rates

Seventy-three percent of women received RT after CS and 13% received chemotherapy as part of their initial treatment course. However, there was significant variation in the utilization of these treatments across the United States, with as little as 50% to as much as 85% utilization of RT after CS by state (P<0.001); while utilization of chemotherapy ranged from 8% to 22% by state (P<0.001) (**Figure 1a, 2a**). After standardization of utilization rates by covariates, significant geographic variation still existed (**Figure 1b, 2b**)**.**

Figure 1a. RT in the United States (all women). Darker shading represents higher percent utilization. Categories: 50% to 60%, 61% to 65%, 66% to 70%, 71% to 73%, 74% to 75%, 76% to 85%, 86% to 100%

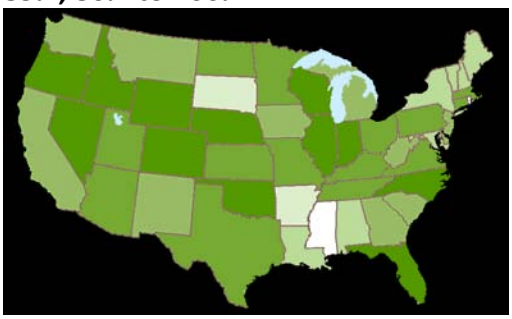


Figure 1b. RT in the United States (standardized risk adjusted rates)

Figure 2a. Chemotherapy in the United States (all women). Categories: 8% to 11%, 12% to 15%, 16% to 18%, 19% to 22%

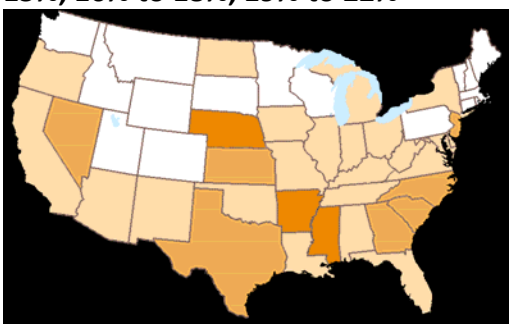


Figure 2b. Chemotherapy in the United States (standardized risk adjusted rates)

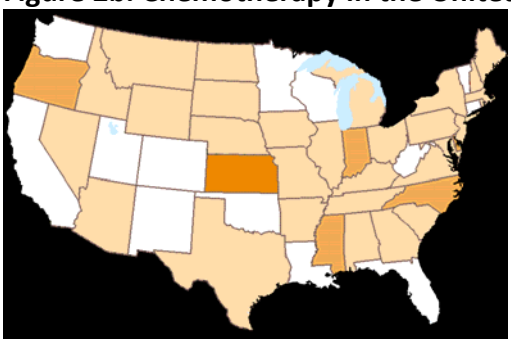
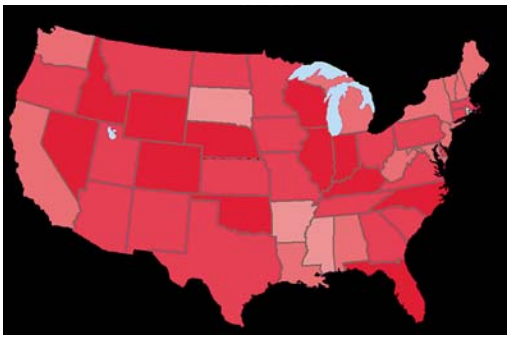


Figure 3. RT use in white women. Categories: 12% to 16%, 17% to 33%, 34% to 50%, 51% to 66%, 67% to 72%, 73% to 75%, 76% to 77%. Gray= data insufficient.



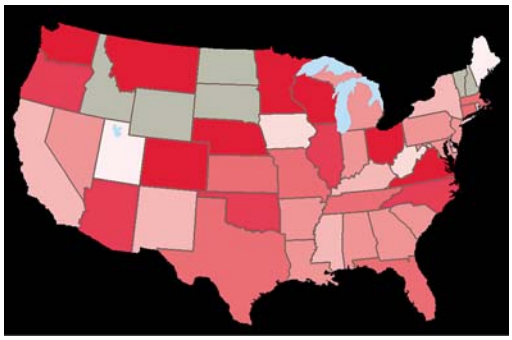


Figure 4. RT use in black women.

Utilization of RT and by race

Significant disparities existed in RT treatment by race, with 74% of white women, 65% of black women, and 66% of other women who received RT after CS (P<0.001) (**Figures 3-4)**. After adjusting for covariates, white women were still significantly more likely than black women to have received RT after CS (Odds Ratio [OR] 1.48, 95% Confidence Interval [CI] 1.34-1.63, P<0.001). There was a trend toward white women also being more likely than other (non-white, non-black) women to have received RT after CS, but this difference was marginally significant (OR= 1.22, 95% CI 1.04-1.42, P=0.01) (**Table 2**).

Table 2. Unadjusted and adjusted utilization of radiotherapy (RT) by race

Model: RT use	OR	95% CI		P
Unadjusted				
White vs. black patients	1.52	1.38	1.67	**<0.001**
White vs. other† patients	1.46	1.27	1.68	**<0.001**
Adjusted*				
White vs. black patients	1.48	1.34	1.63	**<0.001**
White vs. other† patients	1.22	1.04	1.42	**0.01**

* Adjusted for age, comorbidity, chemotherapy (adriamycin or taxol), axillary lymph node involvement, staging imaging, surgeon visits, mammography, physician visits, and region.

Race and utilization in younger patients

In the subset of patients age 70 and younger, in whom RT utilization after CS would be expected to be most common, racial disparities persisted, particularly between white women versus black women. A total of 83% of white women, 72% of black women, and 78% of other women in this younger group received RT after CS (P<0.001). The disparity between white and back women persisted even after adjusting for covariates (OR= 1.81, 95% CI 1.46-2.25, P<0.001).

Race and geographic variation in utilization

There was, however, substantial geographic variation in racial disparities. Regions with the most marked racial disparities included the Pacific West, the East South Central region, and the Northeast (**Table 3**). Black women fared particularly poorly in these regions, with less than 60% RT utilization after CS. (Note that regional and state data were not presented for “other” race due to insufficient numbers of patients in this category).

Table 3. Racial disparities in RT utilization after CS by region

Region	States	% in Whites	% in Blacks	P
Pacific West	CA, OR, WA	72	55	**<0.001**
Mountain West	AZ, CO, ID, MT, NV, NM, UT, WY	76	74	0.81
Midwest, West North Central	IA, KS, MN, MO, NE, ND, SD	74	72	0.77
Midwest, East North Central	IL, IN, MI, OH, WI	76	71	**0.04**
Northeast, New England	CT, ME, MA, NH, NJ, NY, VT	70	58	**<0.001**
Northeast, Mid-Atlantic	DE, DC, MD, PA, RI	72	59	**<0.001**
Southwest, West South Central	AR, LA, OK, TX	73	64	**0.003**
Southeast, East South Central	AL, KY, MS, TN	72	57	**<0.001**
Southeast, South Atlantic	FL, GA, NC, SC, VA, WV	77	69	**<0.001**

Part II (for further details, please see **Annual Report, September 2009)**.

Predictors of BCS versus mastectomy use

The use of BCS was associated with both clinical and non-clinical factors. Patients who were younger, white, and had fewer comorbidities, lymph node-negative disease, and predicted early stage disease were more likely to undergo BCS. Patients who did not receive chemotherapy or did not undergo axillary surgery were also more likely to undergo BCS (**Table 4**). In addition, neighborhood socioeconomic factors were also highly associated with BCS. Specifically, patients living in metropolitan areas and in counties with higher median household income, lower percent living below poverty level, and higher percent with college education were more likely to undergo BCS. Of patients living in non-metropolitan areas, only 51% underwent BCS. Supply of healthcare providers also influenced treatment, with BCS use more likely in patients residing in counties with a higher density of surgeons and radiation oncologists (**Table 4**). Finally, significant geographic variation existed (P<0.001), with patients in the Northeast and Pacific West most likely to undergo BCS. In contrast, patients in the South were least likely to undergo BCS, with half or fewer of all patients in these regions treated with BCS (**Figure 5, Table 5)**. On adjusted analysis, higher density of surgeons was no longer a significant predictor of BCS use (P=0.13), specifically once the multivariate model accounted for geographic region. However, a higher density of radiation oncologists remained a significant predictor of BCS use (P=0.01). (**Table 6**).

Early stage breast cancer subgroup

In the selected subgroup of 43,706 patients with predicted early stage (Stage I or II) disease (77% of the entire sample), a total of 68% (29,828 of 43,706) of this selected group received BCS. This was consistent with a total of 65% (27,544 of 42,499) received BCS in the validation subgroup of patients who did not have axillary involvement and did not receive chemotherapy. Geographic variation persisted in the use of BCS for patients with predicted early stage. Patients in the Northeast (78-79%) and Pacific West (71%) were still the most likely to undergo BCS, while patients in the South (57-59%) and portions of the Midwest (58%) were the least likely (**Table 5**). The validation subgroup was similar, with BCS ranging from 54% (South) to 75% (Northeast). On adjusted analysis, significant predictors of BCS use included

similar demographic, clinical, and socioeconomic factors as predictors for the entire sample (**Table 6**). Significant predictors of BCS use identified in the validation group for early stage breast cancer were also consistent with this analysis.

Table 4. Predictors of treatment utilization

Patient Characteristic	% Treated with BCS (N)	% Treated with Mastectomy (N)	*P*
Demographic			
Age, mean (standard deviation)	76 (7)	77 (7)	**<0.001**
66 to <70 years	63 (7,112)	37 (4,260)	**<0.001**
≥70 years	58 (26,338)	42 (19,015)	
Race			
White	59 (30,572)	41 (20,860)	**<0.001**
Black	54 (2,026)	46 (1,701)	
Other	54 (852)	46 (714)	
Clinical			
Charlson comorbidity score			
0 comorbid conditions	61 (22,735)	39 (14,578)	**<0.001**
1 comorbid condition	57 (6,414)	43 (4,875)	
2 or more comorbid conditions	54 (2,673)	46 (2,314)	
Unknown	52 (1,628)	48 (1,508)	
Disease Stage and Treatment			
Predicted early stage (stage I or II) disease	68 (29,828)	32 (3,622)	**<0.001**
Axillary lymph node positive disease	37 (17,587)	63 (30,050)	**<0.001**
Lymph node-negative disease	63 (5,688)	37 (3,400)	
Axillary lymph node dissection	42 (11,995)	58 (16,715)	**<0.001**
No axillary dissection	77 (21,455)	23 (6,560)	
Radiation therapy	88 (24,823)	12 (3,358)	**<0.001**
No radiation therapy	30 (8,627)	70 (19,917)	
Chemotherapy	44 (4,299)	56 (5,447)	**<0.001**
No chemotherapy	62 (29,151)	38 (17,828)	
Healthcare access*			
Median surgeon density† (IQR)	11 (8-16)	10 (6-15)	**<0.001**
Median radiation oncologist density‡ (IQR)	13 (4-20)	11 (0-19)	**<0.001**
Socioeconomic status*			
Living in metropolitan area	62 (25,979)	38 (16,132)	**<0.001**
Living in non-metropolitan area	51 (7,193)	49 (6,971)	
Median income (IQR)	41,691 (36,221-48,059)	39,879 (34,267-45,922)	**<0.001**
Median percent living in poverty (IQR)	10.7 (8-14)	11.4 (9-14)	**<0.001**
Median percent with college education (IQR)	24 (17-29)	22 (15-28)	**<0.001**

Abbreviations: BCS breast-conserving surgery; IQR interquartile range

* By patient county of residence

† Per 100,000 persons

Figure 5. Percent use of BCS by state (darker shading represents higher frequency of use).

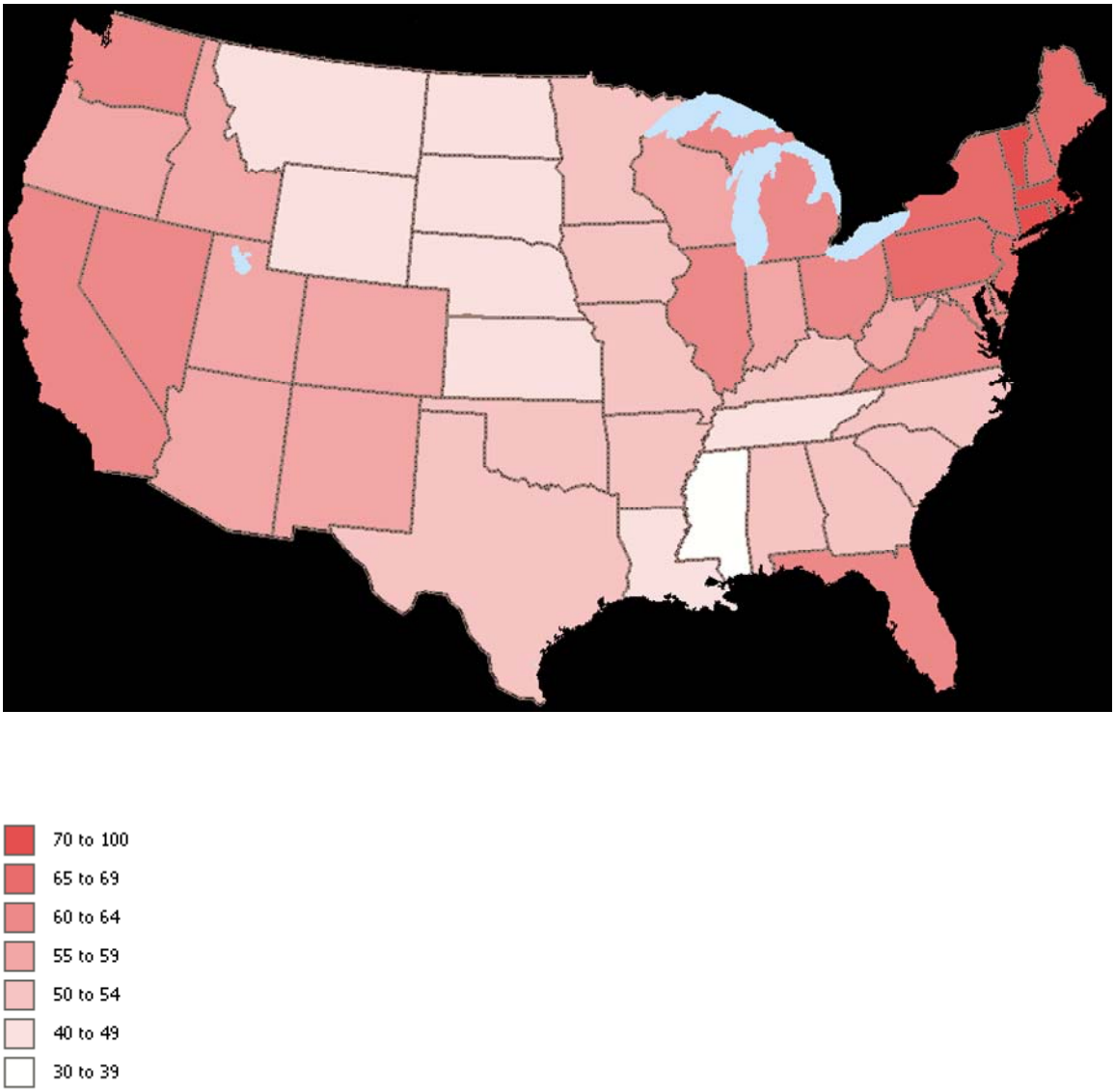


Table 5. Unadjusted and adjusted percent use of breast-conserving surgery (BCS) versus mastectomy by geographic region.

		% BCS (N=23,275)			% Mastectomy (N=33,450)		
Region	**States**	**Overall**	**Adjusted***	**Early Stage**	**Overall**	**Adjusted***	**Early Stage**
West, Pacific West	AK, CA, HI, OR, WA	62	62	71	38	38	29
West, Mountain West	AZ, CO, ID, MT, NV, NM, UT, WY	57	58	66	43	42	34
Midwest, West North Central	IA, KS, MN, MO, NE, ND, SD	50	51	58	50	49	41
Midwest, East North Central	IL, IN, MI, OH, WI	61	60	70	39	40	30
Northeast, New England	CT, MA, NH, ME, RI, VT	70	63	79	30	36	21
Northeast, Mid-Atlantic	NJ, NY, PA	67	64	78	33	35	22
South, South Atlantic	DE, DC, FL, GA, MD, NC, SC, VA, WV	59	59	68	41	41	32
South, West South Central	AK, LA, OK, TX	50	54	59	50	45	41
South, East South Central	AL, KY, MS, TN	48	51	57	52	48	43

Abbreviations: BCS breast-conserving surgery

* Adjusted for covariates including age, race, comorbidity score, axillary lymph node involvement, axillary dissection, chemotherapy, screening mammography, physician visits, surgeon density, radiation oncologist density, metropolitan area, poverty, education.

Table 6. Multivariate logistic model: Predictors of utilization of breast-conserving surgery.

	Entire sample				Early stage subgroup			
Covariate	**OR**	**95% CI**		***P***	**OR**	**95% CI**		***P***
Age 66 to <70 years vs. ≥70 years	1.37	1.31	1.44	**<0.001**	1.15	1.09	1.22	**<0.001**
Race								
White vs. black race	1.14	1.05	1.23	**<0.001**	0.95	0.86	1.04	0.26
White vs. other race	1.29	1.15	1.45	**<0.001**	1.17	1.08	1.27	**<0.001**
Charlson comorbidity score								
0 vs. 1 comorbid conditions	1.18	1.13	1.24	**<0.001**	1.21	1.15	1.28	**<0.001**
0 vs. 2 or more comorbid conditions	1.38	1.29	1.47	**<0.001**	1.17	1.08	1.27	**<0.001**
0 vs. unknown comorbid conditions	1.12	1.01	1.25	**0.03**	0.91	0.79	1.05	0.20
Lymph node-negative disease	1.60	1.52	1.68	**<0.001**	-	-	-	-
No axillary lymph node dissection*	4.00	3.85	4.17	**<0.001**	4.65	4.46	4.88	**<0.001**
No chemotherapy*	1.32	1.25	1.39	**<0.001**	0.63	0.57	0.69	**<0.001**
Screening mammography§	2.02	1.87	2.17	**<0.001**	0.89	0.80	1.00	**0.04**
1 or more visits to physician§	1.43	1.22	1.68	**<0.001**	1.97	1.60	2.43	**<0.001**
Geographic Region[II]								
West, Pacific West	0.86	0.78	0.95	**0.008**	0.81	0.72	0.92	**0.001**
West, Mountain West	0.71	0.63	0.80	**<0.001**	0.69	0.60	0.80	**<0.001**
Midwest, West North Central	0.50	0.45	0.55	**<0.001**	0.45	0.40	0.51	**<0.001**
Midwest, East North Central	0.80	0.73	0.88	**<0.001**	0.75	0.67	0.84	**<0.001**
Northeast, Mid-Atlantic	1.05	0.95	1.16	0.34	1.06	0.94	1.19	0.36
South, South Atlantic	0.76	0.69	0.83	**<0.001**	0.69	0.62	0.78	**<0.001**
South, West South Central	0.58	0.53	0.65	**<0.001**	0.54	0.48	0.61	**<0.001**
South, East South Central	0.51	0.45	0.57	**<0.001**	0.45	0.39	0.52	**<0.001**
Surgeon density†	1.00	0.99	1.01	0.13	1.00	0.99	1.01	0.14
Radiation oncologist density§	1.30	1.06	1.59	**0.01**	1.37	1.07	1.75	**0.01**
Living in metropolitan area	1.20	1.14	1.26	**<0.001**	1.20	1.13	1.27	**<0.001**
Percent living in poverty < 11%[I]	1.05	1.00	1.09	**0.03**	1.05	1.00	1.11	0.06
Percent with college education > 23%[I]	1.13	1.08	1.19	**<0.001**	1.15	1.09	1.21	**<0.001**

Abbreviations: CI confidence interval, OR odds ratio

* A model excluding axillary lymph node dissection and chemotherapy, which are treatments likely to occur concurrently or after surgery, did not affect risk estimates for other covariates.

† Increased odds per 1 surgeon per 100,000 persons

§ Increased odds per 1 radiation oncologist per 10,000 persons

[I] Continuous variables dichotomized at the median value

[II] Compared with reference category Northeast New England. The Likelihood ratio test for all strata of the variable for region was statistically significant (P<0.001).

Part III

Costs of cancer and non-cancer care

In the year following diagnosis, the median breast cancer care-related costs (as reimbursed by Medicare) was $6,101 (interquartile range [IQR] $2,900 to $13,058). The most costly contributor to these costs was surgery-related costs (**Table 7**). These cancer-related costs compare with the median overall health care costs of $12,274 (IQR $7,623 to $19,041) and median non-cancer-related costs of $4,376 (IQR $668 to $9042). There was a significant correlation between cancer-related costs and overall health care costs in our sample (Pearson's R= 0.56, P<0.001).

Table 7. Median costs of breast cancer care

Category	Median costs ($)	IQR	Mean(SD)
Total breast cancer-related costs	6,101	2,900 - 13,058	9,973 (11,726)
Surgery			
Breast conserving surgery	411	163 - 865	727 (1,400)
Mastectomy	626	163 - 1,017	1,098 (1,783)
Axillary treatment	643	212 - 1,086	1,097 (2,007)
Reconstruction	1,045	210 - 2,171	1,511 (1,729)
Chemotherapy	895	205 - 3,401	2,524 (4,055)
Radiotherapy	2,042	1,105 - 4,489	3,136 (3,329)
Other/ Unspecified	3,344	1,597 - 6,859	5,770 (7,471)

Abbreviations: IQR interquartile range, SD standard deviation

Our data further demonstrated that there was significant geographic variation in breast cancer-related costs (P<0.001) (**Table 8**, **Figure 6**). In particular, there appeared to be lower cancer-related spending in the Southeastern region of the US and parts of the Midwestern US (**Table 8**) (P<0.001). This geographic variation appeared to correlate with variation in overall healthcare costs, with overall spending also lowest in the Southeastern US.

Other predictors were also found to have a significant correlation with breast cancer-related costs on univariate analysis. Not surprisingly, treatment utilization with any treatment modality (surgery, chemotherapy, or radiotherapy) was associated with increased costs. In addition, other clinical variables showed strong associations, including indicators of greater disease involvement such as axillary disease (nodal involvement). Patient factors also were associated, with younger women with fewer comorbidities more likely to incur breast cancer related costs. Interestingly, however, socioeconomic variables also demonstrated associations, with patients who were white, had higher income and higher education, and lived in a metropolitan area more likely to incur breast cancer related costs (**Table 9**). These variables remained significant on multivariate analysis.

Table 8. Geographic variation in breast cancer-related costs and overall costs (in $).

	Breast Cancer-Related			Overall		
States	**Median ($)**	**IQR 25th**	**IQR 75th**	**Median ($)**	**IQR 25th**	**IQR 75th**
AK, CA, HI, OR, WA	6,367	2,993	13,166	13,079	8,224	19,452
AZ, CO, ID, MT, NV, NM, UT, WY	6,480	3,108	13,409	11,875	7,561	17,971
IA, KS, MN, MO, NE, ND, SD	5,076	2,636	11,368	10,885	6,501	16,094
IL, IN, MI, OH, WI	5,993	2,971	12,817	12,255	7,770	18,719
CT, MA, NH, ME, RI, VT	6,025	2,993	12,933	12,596	8,616	17,650
NJ, NY, PA	6,568	2,962	13,677	13,474	8,662	20,748
DE, DC, FL, GA, MD, NC, SC, VA, WV	6,300	2,997	13,797	12,656	7,837	20,219
AK, LA, OK, TX	6,541	2,919	13,112	11,612	7,069	19,207
AL, KY, MS, TN	5,018	2,424	11,502	10,804	6,304	16,785

Figure 6. Breast-cancer related costs across the United States

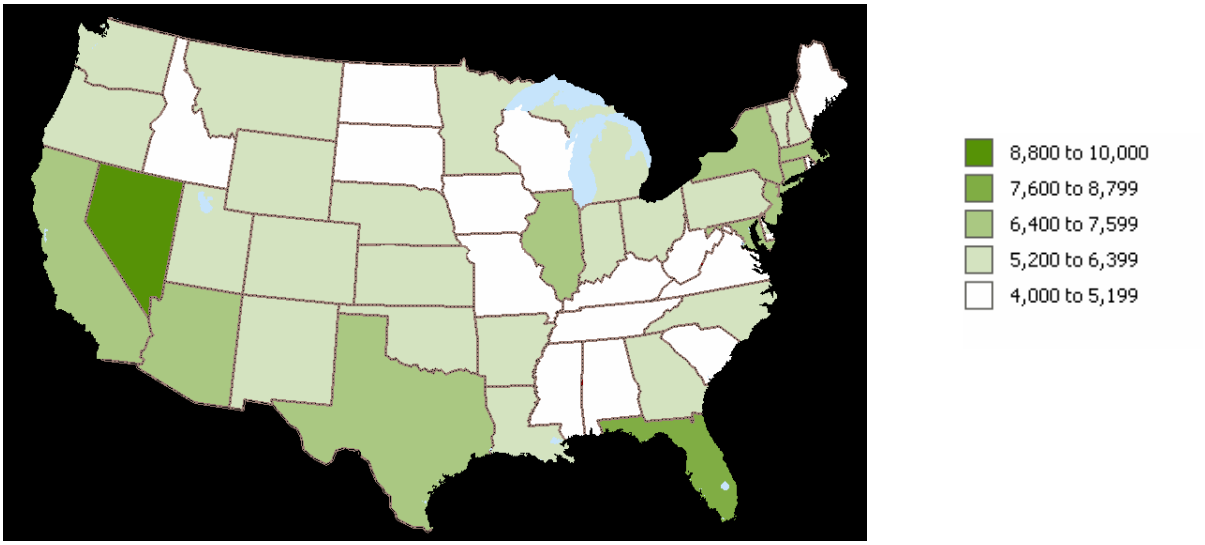


Table 9. Predictors of breast cancer-related spending

Patient Characteristic	Median Cost ($)	*P*
Demographic		
Age		
66 to <70 years	8,120	**<0.001**
≥70 years	5,670	
Race		
White	6,123	**0.03**
Black	5,952	
Other	5,766	
Clinical		
Charlson comorbidity score		
0 comorbid conditions	6,077	**<0.001**
1 comorbid condition	5,675	
2 or more comorbid conditions	5,887	
Unknown	9,652	
Disease Stage and Treatment		
Breast-conserving surgery	7,132	**<0.001**
Mastectomy	4,530	
Axillary lymph node positive disease	12,022	**<0.001**
Lymph node-negative disease	5,514	
Axillary lymph node dissection	7,564	**<0.001**
No axillary dissection	4,885	
Post-mastectomy reconstruction	8,890	**<0.001**
No post-mastectomy reconstruction	6,037	
Radiation therapy	10,087	**<0.001**
No radiation therapy	3,208	
Chemotherapy	18,512	**<0.001**
No chemotherapy	5,012	
Healthcare access*		
Surgeon density† (Pearson's R)	0.00036	0.93
Radiation oncologist density‡ (Pearson's R)	0.016	**0.0002**
Socioeconomic status*		
Living in metropolitan area	6,326	**<0.001**
Living in non-metropolitan area	5,371	
Income (Pearson's R)	0.034	**<0.001**
Percent with college education (Pearson's R)	0.021	**<0.001**

Abbreviations: BCS breast-conserving surgery

* Defined by patient county of residence

† Per 100,000 persons

‡ Per 10,000 persons

Brachytherapy utilization and pilot longitudinal subgroup

Of all patients from the national Medicare dataset treated BCS, 97% were treated with external beam radiotherapy (EBRT) alone, 3% with brachytherapy alone, and <1% with EBRT plus brachytherapy boost. For patients treated with brachytherapy, 98% received interstitial therapy and 2% intracavitary therapy. Though percent utilization of brachytherapy modalities ranged from 1% to 4% across different locations in the US, no statistically significant variation was detected by state (P=0.62) or by region (P=0.32). In addition, brachytherapy use did not differ by race (P=0.63) or age (P=0.59).

Of the entire sample, 5% (333 of 6,882) received brachytherapy alone (multi-catheter or balloon-based), 95% (6,521 of 6,882) received EBRT, and <1% (28 of 6,865) received EBRT plus brachytherapy boost. Treatments with brachytherapy alone significantly increased over time, from <1% in 2001, 2% in 2002, 3% in 2003, 5% in 2004, 8% in 2005, and 10% in 2006 (P<0.001) (**Table 10**). The most notable increases could be benchmarked against two major policy events: First, an increase in use was noted after July 2002, correlating with FDA approval of the balloon-based breast brachytherapy device (June 2002); and also, a further increase was noted after July 2004, correlating with Medicare reimbursement of treatment (April 2004) (**Figure 7**). Of patients treated with any form of brachytherapy alone, the proportion who received balloon-based treatment also increased dramatically over time, with 89% receiving balloon-based treatment by 2006 (**Figure 8**). In multivariate analysis, the temporal trend indicating a steady increase in the use of brachytherapy remained significant (P<0.001).

Table 10. Temporal trends in brachytherapy utilization

Time period	Total	% with EBRT only	(N)	% with EBRT + Boost	(N)	% Brachytherapy only	(N)
1/1/2001 – 6/30/2001	183	98.91	181	0.00	0	1.09	2
7/1/2001 – 12/30/2001	363	98.90	359	0.55	2	0.55	2
1/1/2002 – 6/30/2002	469	99.36	466	0.21	1	0.43	2
7/1/2002 – 12/30/2002	494	96.76	478	0.20	1	3.04	15
1/1/2003 – 6/30/2003	711	97.19	691	0.14	1	2.67	19
7/1/2003 – 12/30/2003	828	96.14	796	0.48	4	3.38	28
1/1/2004 – 6/30/2004	874	94.62	827	0.34	3	5.03	44
7/1/2004 – 12/30/2004	851	94.48	804	0.24	2	5.29	45
1/1/2005 – 6/30/2005	942	91.83	865	0.85	8	7.32	69
7/1/2005 – 12/30/2005	534	91.57	489	0.37	2	8.05	43
1/1/2006 – 6/30/2006	633	89.26	565	0.63	4	10.11	64
Total	6882	94.75	6521	0.41	28	4.83	333

Figure 7. Temporal trends: Percent of patients treated with brachytherapy (multi-catheter or balloon-based) as the sole modality of radiotherapy after breast-conserving therapy. Year 'a' refers to January through June and 'b' July through December. (P<0.001)

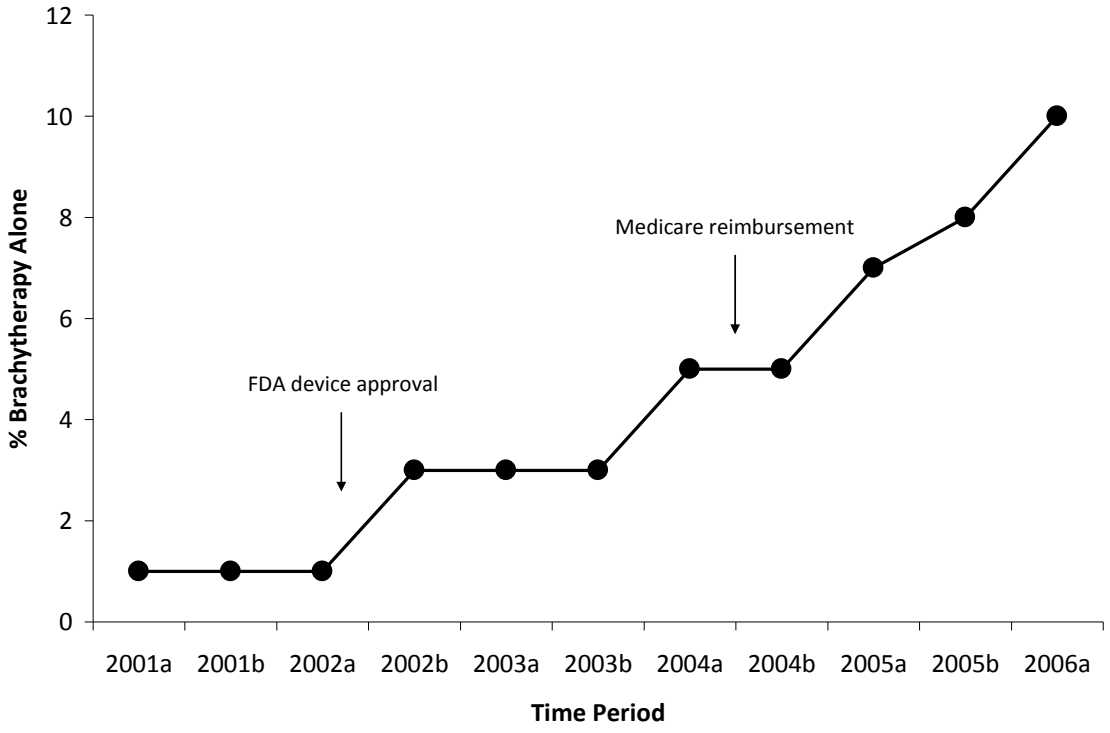
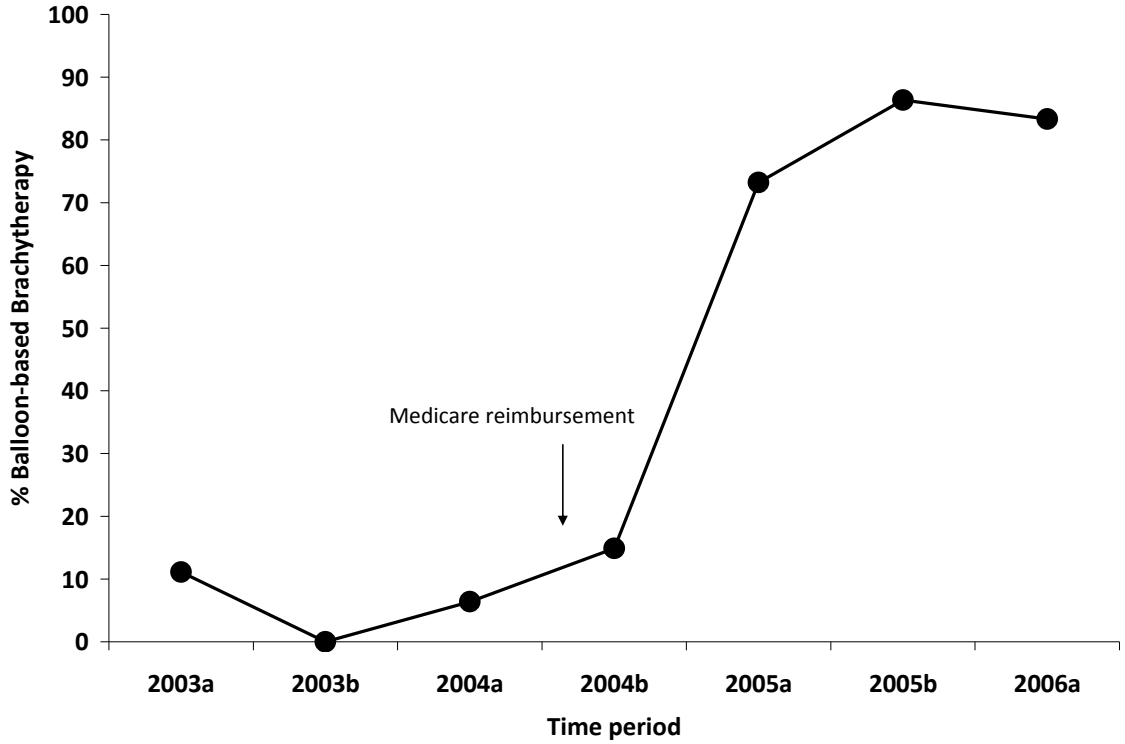


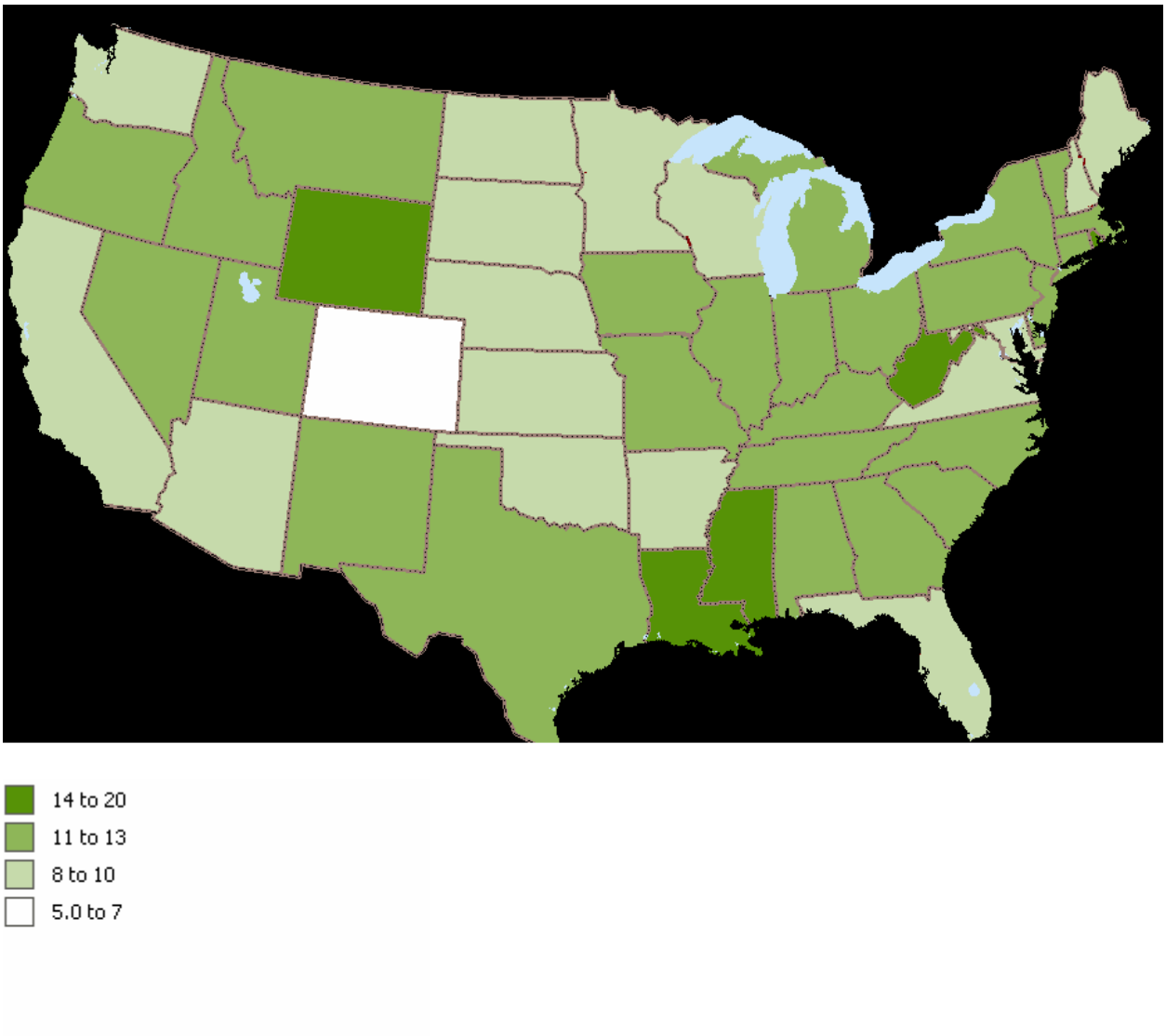
Figure 8. Temporal trends: Percent of patients treated with brachytherapy as the sole modality of radiotherapy after breast-conserving therapy that received balloon-based brachytherapy. Year 'a' refers to January through June and 'b' July through December. (P<0.001)



Part IV

Survival. In the longitudinal cohort of women treated with BCS, of 62,625 patients, by the end of the follow-up period, a total of 11% of patients had died (n=6,705). For those who died, the median time to death was 709 days (IQR 445, 1049). Survival was significantly associated with the use of RT after BCS. Sixty-four percent of all patients received RT over the study period. Of patients who received RT, 17% died, compared with 7% of those who did not receive RT (P<0.001). Survival rates varied significantly by state (P<0.001) and geographic region (P<0.001, **Figure 9**).

Figure 9. Percent died. Darker shading represents a higher percentage of patients who died.



Notably, high death rates (and thus low survival rates) were still found in areas of the South and Midwest, areas which had also previously demonstrated lower rates of appropriate treatment utilization. The Northeast also showed higher death rates on unadjusted analysis.

On multivariate analysis, younger age and white race were associated with better overall survival. In addition, use of RT was associated with better survival (OR= 0.50, 95% CI 0.48, 0.53). Interestingly, even after adjusting for these covariate factors, geographic region remained a significant predictor (**Table 11**).

Table 11. Adjusted and unadjusted survival by region

Region	States	% Died	OR	95% CI	
West, Pacific West	AK, CA, HI, OR, WA	11	-	-	-
West, Mountain West	AZ, CO, ID, MT, NV, NM, UT, WY	10	1.23	1.06	1.41
Midwest, West North Central	IA, KS, MN, MO, NE, ND, SD	10	1.18	1.04	1.34
Midwest, East North Central	IL, IN, MI, OH, WI	12	1.41	1.28	1.55
Northeast, New England	CT, MA, NH, ME, RI, VT	11	1.30	1.15	1.47
Northeast, Mid-Atlantic	NJ, NY, PA	12	1.28	1.16	1.41
South, South Atlantic	DE, DC, FL, GA, MD, NC, SC, VA, WV	11	1.26	1.15	1.39
South, West South Central	AK, LA, OK, TX	11	1.28	1.13	1.45
South, East South Central	AL, KY, MS, TN	12	1.43	1.24	1.64

Discussion

Summary, Comments, and Future Work

In this contemporary, national cohort of older breast cancer patients, we demonstrated the following novel findings:

- Significant geographic (regional) variation existed for the use of chemotherapy and RT. Furthermore, even though multivariate adjustment attempted to adjust for variations in case-mix across the United States, geographic variation was still a significant predictor of treatment choices.
- For the use of RT after BCS, a significant amount of variation also existed. The absolute frequency of underutilization of RT was also surprising, as high as 27% across the country and even as high as 50% in some states. Racial differences in utilization were also significant.
- The use of breast conservation for early invasive disease also significantly varied. Use of BCS was as low as approximately 50% in some regions of the United States, and was associated with socioeconomic factors, suggesting that socioeconomic barriers have a significant effect on the use of breast conservation.
- Clinical and non-clinical variations in breast cancer-related costs were also of interest. Increased spending appeared to reflect adherence to standard treatment (for example, the use of RT after BCS) and higher socioeconomic status.
- Use of newer therapies was also associated with both clinical and non-clinical factors, with both patient and physician factors contributing. Interestingly, some socioeconomic and policy factors may overshadow clinical efficacy data in influencing physician or patient behavior in selecting treatments for breast cancer.
- Survival was associated with use of RT after BCS. However, survival varied significantly by region. While regional patterns resembled utilization patterns, still utilization (or underutilization) of standard care could not fully explain differences in survival across the United States.

Please see **Annual Reports, September 2008 and September 2009**, for any further detailed discussion of these points.

The body of work that we have produced from our analyses has provided a unique contribution to the literature. Strengths of our project include the use of a novel dataset, the national Medicare dataset. This is one of the largest cohorts assembled to date. Our long-term goal of obtaining near and long-term follow-up allows our dataset to be one of the most unique for studying the course of both treatment and outcomes in breast cancer patients. Finally, we contributed to gaps in the literature on disparities in breast cancer care. We demonstrated and quantified persistent disparities, particularly for the use of surgery and radiation therapy in breast cancer patients. In addition, however, using one of the unique strengths of the Medicare dataset—the comprehensive information provided on all beneficiaries across the United States—we were able to study in detail the geographic variations of the disparities. The significance and the absolute magnitude of these variations were staggering.

Our results prompt several areas of future directions and needs in the area of investigating disparities in breast cancer care. While we were able to detail the magnitude of disparities and regional variation in treatment, cost, and outcomes using our Medicare dataset, future investigations may focus on what are the underlying causes of regional differences. We hypothesize, in part prompted by our hypothesis-generating results, that both physician and patient influences– and consideration of the patient-physician interaction– may be contributory. Of importance is understanding these potential factors and being able to take into account individual, regional, or cultural preferences for care when determining treatment goals. Another important question that our results prompt is, what are the best strategies that may be applied to overcome real socioeconomic barriers that clearly continue to affect treatment utilization across the United States? Our finding of socioeconomic barriers to breast conservation in our contemporary cohort suggest that little progress has been made in overcoming disparities in the use of breast conserving therapy, particularly for patients living in the most disadvantaged neighborhoods and regions. Future research may explore whether interventions at the individual patient level, combined with changes at the policy level, may help to overcome barriers to quality breast cancer care. Finally, our investigations have focused on older patients, and these data should be validated in populations of younger breast cancer patients as well. The implications of answering these questions are on the ever-present demands to simultaneously optimize treatment quality, effectiveness and costs. It is hoped that the insights gained in this area of research may help to improve the rationale by which therapies are promoted and adopted into standard care.

KEY RESEARCH ACCOMPLISHMENTS

- Assembled a unique, contemporary cross-sectional Medicare breast cancer cohort
- Assembed a unique, longitudinal Medicare breast cancer cohort with follow-up
- Obtained and analyzed treatment utilization in several validation populations, including SEER-Medicare and MarketScan databases.
- Developed, applied, and validated unique algorithms for identifying breast cancer patients and early stage subgroup of patients based on claims data.
- Conducted univariate and multivariate data analyses on treatment utilization, cost, and outcomes in breast cancer patients.
- Further conducted stratified and subsidiary analyses, including an analysis of the disparities in treatment and costs by clinical and non-clinical factors
- Publication of multiple manuscripts and preparation of manuscripts in progress, at peer-reviewed journals
- Presentation of results at national scientific meetings

REPORTABLE OUTCOMES

Manuscripts (for full listing, please see Appendix, CV)

1. **Smith GL**, Shih YT, Giordano SH, Smith BD, Buchholz TA. Predicting breast cancer tumor stage using Medicare claims data. 2009. Epidemiologic Perspectives & Innovations 2010 Jan; 7:1.

2. **Smith GL,** Xu Y, Shih YCT, Giordano SH, Smith BD, Hunt KK, Strom EA, Perkins GH, Hortobagyi GN, Buchholz TA.. Breast-conserving surgery in older patients with invasive breast cancer: Current patterns of treatment across the United States. J Am Coll Surg. 2009 Oct;209(4):425-433.

3. **Smith GL,** Shih YT, Xu Y, Giordano SH, Smith BD, Perkins G, Tereffe W, Woodward WA, Buchholz TA. Racial disparities in treatment for early invasive breast cancer: a national Medicare study of radiotherapy after conservative surgery. Cancer 2010 Feb 1;116(3):734-41.

4. Smith BD, **Smith GL**, Hurria A, Buchholz TA. The future of cancer incidence in the United States: Expected burdens upon an aging, changing nation. J Clin Oncol. 2009 Jun 10;27(17):2758-65.

5. **Smith GL**, Smith BD, Garden AS, Rosenthal DI, Sherman SI, Morrison WH, Schwartz DL, Weber RS, Buchholz TA. Hypothyroidism in older head and neck cancer patients after treatment with radiation: A population-based study. Head and Neck 2009 Aug;31(8):1031-8.

6. Smith BD, **Smith GL**, Roberts KB, Buchholz TA. Baseline utilization of breast radiotherapy prior to institution of the Medicare Practice Quality Reporting Initiative. Int J Radiat Oncol Biol Phys 2009 Aug 1;74(5):1506-12

7. **Smith GL,** Smith BD, Buchholz TA, Liao Z, Jeter M, Swisher SG, Hofstetter WL, Ajani JA, Komaki R, Cox JD. Patterns of care and local-regional treatment outcomes in older esophageal cancer patients. Int J Radiat Oncol Biol Phys. 2009 Jun 1;74(2):482-9

8. **Smith GL**, Smith BD, Buchholz TA, Giordano S, Frank S, Schwartz D, Garden A, Morrison W, Chao C, Woodward WA, Yom S, Weber R, Ang KK, Rosenthal D. Cerebrovascular disease risk in older head and neck cancer patients treated with radiation therapy. J Clin Oncol. 2008 Nov 1;26(31):5119-25. *Highlighted in Cogent Medicine Radiation Oncology, October 2008

9. **Smith GL**, Smith BD, Giordano SH, Shih YC, Woodward WA, Strom EA, Perkins GH, Tereffe W, Yu T, Buchholz TA. Risk of hypothyroidism in older breast cancer patients treated with radiation. Cancer 2008 Mar 15;112(6):1371-9.

10. Smith BD, Haffty BG, **Smith GL**, Hurria A, Buchholz TA, Gross CP. Utilization of Post-Mastectomy Radiation in Older Women. Int J Radiat Oncol Biol Phys 2008 May 1;71(1):98-106.

Abstracts and presentations

1. **Smith GL**, Xu Y, Buchholz TA, Smith BD, Giordano SH, Shih YCT. Breast brachytherapy in the United States: utilization patterns in older patients after breast-conserving surgery. Abstract 2009. (Oral presentation: American Society of Therapeutic Radiology and Oncology). Also presented at CDMRP-LINKS meeting, as a poster, February 2010.

2. **Smith GL**, Shih YT, Xu Y, Giordano SH, Smith BD, Buchholz TA. Breast brachytherapy in the United States: How is this emerging modality being incorporated into the care of older breast cancer patients? Abstract 2008. (Poster presentation: San Antonio Breast Cancer Symposium). Also presented at CDMRP-LINKS meeting, February 2009.

3. **Smith GL**, Shih YT, Xu Y, Giordano SH, Smith BD, Perkins GH, Tereffe W, Woodward WA, Buchholz TA. Racial disparities in treatment for early invasive breast cancer: A national Medicare study of radiotherapy after conservative surgery. Abstract 2008. (Poster presentation: American Society of Clinical Oncology 2008 Breast Cancer Symposium). Highlighted by Medscape Oncology, Reuters, Healthday news, Houston Chronicle, and Houston public radio.

4. **Smith GL**, Smith BD, Giordano SH, Shih YC, Woodward WA, Strom EA, Perkins GH, Oh JL, Tereffe W, Buchholz TA. Risk of hypothyroidism in older breast cancer patients treated with radiotherapy. Abstract 2007 (Poster presentation: American Society for Therapeutic Radiology and Oncology). Also presented at Era of Hope meeting, 2008.

Awards and Recognition

July 2009 Smith GL, et al. "Breast-conserving surgery in older patients with invasive breast cancer: Current patterns of treatment across the United States" manuscript to be highlighted in the October continuing medical education (CME) issue of J Am Coll Surg

2008	American Society of Clinical Oncology (ASCO) Breast Cancer Symposium Merit Award
2008	M. D. Anderson Cancer Center Odyssey Fellow Award, to support the best postdoctoral trainees among the newest generation of cancer researchers at the institution
2008	Susan G. Komen Houston Affiliate Travel Scholarship, to support participation at the American Society of Clinical Oncology 2008 Breast Cancer Symposium

Updated CV, SEE APPENDIX.

Reprints of manuscripts, SEE APPENDIX.

Note: Smith GL et al. Epidemiologic Perspectives & Innovations 2010 Jan; 7:1 is available at http://www.epi-perspectives.com/content/7/1/1.

CONCLUSION

At the conclusion of Year 3 of our research, we have made significant progress toward accomplishing our project goals. Specifically, we have worked to accomplish the objectives stated for Year 3 in the Statement of Work. Using our novel, comprehensive national Medicare dataset, we conducted several retrospective analyses on a cohort of older women diagnosed with early invasive breast cancer. Results from our analyses provided novel insights that contribute to the existing scientific literature. The most striking results from our analyses suggest that variation in breast cancer care is significant, and these variations appear to contribute to variations in costs and outcomes for breast cancer care across the United States.

REFERENCES

1. Malin JL, Schneider EC, Epstein AM, Adams J, Emanuel EJ, Kahn KL. Results of the National Initiative for Cancer Care Quality: how can we improve the quality of cancer care in the United States? *J Clin Oncol.* Feb 1 2006;24(4):626-634.
2. Gross CP, Smith BD, Wolf E, Andersen M. Racial disparities in cancer therapy: did the gap narrow between 1992 and 2002? *Cancer.* Feb 15 2008;112(4):900-908.
3. Smith BD, Arthur DW, Buchholz TA, et al. American Society of Therapeutic Radiology and Oncology Consensus Statement on Accelerated Partial Breast Irradiation. *Int J Radiat Oncol Biol Phys.* In press. 2009.
4. Nattinger AB, Laud PW, Bajorunaite R, Sparapani RA, Freeman JL. An algorithm for the use of Medicare claims data to identify women with incident breast cancer. *Health Serv Res.* Dec 2004;39(6 Pt 1):1733-1749.
5. Gold HT, Do HT. Evaluation of three algorithms to identify incident breast cancer in Medicare claims data. *Health Serv Res.* Oct 2007;42(5):2056-2069.
6. Smith BD, Gross CP, Smith GL, Galusha DH, Bekelman JE, Haffty BG. Effectiveness of radiation therapy for older women with early breast cancer. *J Natl Cancer Inst.* May 17 2006;98(10):681-690.
7. Smith BD, Haffty BG, Buchholz TA, et al. Effectiveness of radiation therapy in older women with ductal carcinoma in situ. *J Natl Cancer Inst.* Sep 20 2006;98(18):1302-1310.
8. Smith BD, Haffty BG, Smith GL, Hurria A, Buchholz TA, Gross CP. Use of postmastectomy radiotherapy in older women. *Int J Radiat Oncol Biol Phys.* May 1 2008;71(1):98-106.
9. Smith BD, Smith GL, Buchholz TA. Controversies over the role of radiation therapy for ductal carcinoma in situ. *Expert Rev Anticancer Ther.* Mar 2008;8(3):433-441.
10. Smith BD, Smith GL, Haffty BG. Postmastectomy radiation and mortality in women with T1-2 node-positive breast cancer. *J Clin Oncol.* Mar 1 2005;23(7):1409-1419.
11. Smith GL, Smith BD, Giordano SH, et al. Risk of hypothyroidism in older breast cancer patients treated with radiation. *Cancer.* Mar 15 2008;112(6):1371-1379.
12. Klabunde CN, Potosky AL, Legler JM, Warren JL. Development of a comorbidity index using physician claims data. *J Clin Epidemiol.* Dec 2000;53(12):1258-1267.
13. US Census Bureau. http://www.census.gov. Last accessed March 2009. Accessed September, 2008.
14. Health Resources and Services Administration. Area Resource File. http://www.arfsys.com/overview.htm. Last accessed February 2009.
15. Smith G, Shih Y, Giordano S, Smith B, Buchholz T. A Method to Predict Breast Cancer Stage Using Medicare Claims. *In submission.* 2009.
16. Consensus statement: treatment of early-stage breast cancer. National Institutes of Health Consensus Development Panel. *J Natl Cancer Inst Monogr.* 1992(11):1-5.
17. Fisher B, Bauer M, Margolese R, et al. Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer. *N Engl J Med.* Mar 14 1985;312(11):665-673.
18. Nattinger AB, Gottlieb MS, Veum J, Yahnke D, Goodwin JS. Geographic variation in the use of breast-conserving treatment for breast cancer. *N Engl J Med.* Apr 23 1992;326(17):1102-1107.
19. Gilligan MA, Kneusel RT, Hoffmann RG, Greer AL, Nattinger AB. Persistent differences in sociodemographic determinants of breast conserving treatment despite overall increased adoption. *Med Care.* Mar 2002;40(3):181-189.
20. Freedman RA, He Y, Winer EP, Keating NL. Trends in racial and age disparities in definitive local therapy of early-stage breast cancer. *J Clin Oncol.* Feb 10 2009;27(5):713-719.
21. Morrow M, White J, Moughan J, et al. Factors predicting the use of breast-conserving therapy in stage I and II breast carcinoma. *J Clin Oncol.* Apr 15 2001;19(8):2254-2262.
22. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med.* Oct 17 2002;347(16):1233-1241.
23. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med.* Oct 17 2002;347(16):1227-1232.

24. Katipamula R, Hoskin TL, Boughey JC. Trends in mastectomy rates at the Mayo Clinic Rochester: Effect of surgical year and pre-operative MRI. *Proceedings from the 44th annual meeting of the American Society of Clinical Oncology. Chicago, IL.* 2008;Abstract #509.
25. McCarthy EP, Ngo LH, Roetzheim RG, et al. Disparities in breast cancer treatment and survival for women with disabilities. *Ann Intern Med.* Nov 7 2006;145(9):637-645.
26. Baldwin LM, Taplin SH, Friedman H, Moe R. Access to multidisciplinary cancer care: is it linked to the use of breast-conserving surgery with radiation for early-stage breast carcinoma? *Cancer.* Feb 15 2004;100(4):701-709.
27. Voti L, Richardson LC, Reis IM, Fleming LE, Mackinnon J, Coebergh JW. Treatment of local breast carcinoma in Florida: the role of the distance to radiation therapy facilities. *Cancer.* Jan 1 2006;106(1):201-207.
28. Clarke M, Collins R, Darby S, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. *Lancet.* Dec 17 2005;366(9503):2087-2106.
29. Jatoi I, Proschan MA. Randomized trials of breast-conserving therapy versus mastectomy for primary breast cancer: a pooled analysis of updated results. *Am J Clin Oncol.* Jun 2005;28(3):289-294.
30. McCormick B. Partial-breast radiation for early staged breast cancers: hypothesis, existing data, and a planned phase III trial. *J Natl Compr Canc Netw.* May 2005;3(3):301-307.
31. Offersen BV, Overgaard M, Kroman N, Overgaard J. Accelerated partial breast irradiation as part of breast conserving therapy of early breast carcinoma: a systematic review. *Radiother Oncol.* Jan 2009;90(1):1-13.
32. Vicini F, Beitsch PD, Quiet CA, et al. Three-year analysis of treatment efficacy, cosmesis, and toxicity by the American Society of Breast Surgeons MammoSite Breast Brachytherapy Registry Trial in patients treated with accelerated partial breast irradiation (APBI). *Cancer.* Feb 15 2008;112(4):758-766.
33. Chen PY, Vicini FA, Benitez P, et al. Long-term cosmetic results and toxicity after accelerated partial-breast irradiation: a method of radiation delivery by interstitial brachytherapy for the treatment of early-stage breast carcinoma. *Cancer.* Mar 1 2006;106(5):991-999.
34. King TA, Bolton JS, Kuske RR, Fuhrman GM, Scroggins TG, Jiang XZ. Long-term results of wide-field brachytherapy as the sole method of radiation therapy after segmental mastectomy for T(is,1,2) breast cancer. *Am J Surg.* Oct 2000;180(4):299-304.
35. Krishnan L, Jewell WR, Tawfik OW, Krishnan EC. Breast conservation therapy with tumor bed irradiation alone in a selected group of patients with stage I breast cancer. *Breast J.* Mar-Apr 2001;7(2):91-96.
36. Kuske RR, Winter K, Arthur DW, et al. Phase II trial of brachytherapy alone after lumpectomy for select breast cancer: toxicity analysis of RTOG 95-17. *Int J Radiat Oncol Biol Phys.* May 1 2006;65(1):45-51.
37. Perera F, Yu E, Engel J, et al. Patterns of breast recurrence in a pilot study of brachytherapy confined to the lumpectomy site for early breast cancer with six years' minimum follow-up. *Int J Radiat Oncol Biol Phys.* Dec 1 2003;57(5):1239-1246.
38. Abelson R. Quickly vetted, treatment is offered to patients. *The New York Times*, 2008.
39. Sher DJ, Wittenberg E, Suh WW, Taghian AG, Punglia RS. Partial-breast irradiation versus whole-breast irradiation for early-stage breast cancer: a cost-effectiveness analysis. *Int J Radiat Oncol Biol Phys.* Jun 1 2009;74(2):440-446.

APPENDIX. CURRICULUM VITAE

Grace Li Smith, M.D., Ph.D., M.P.H.

Education and Training

2007-present	**University of Texas M.D. Anderson Cancer Center**, Houston, TX Postdoctoral Fellow, Department of Radiation Oncology Odyssey Fellow, 2008-present
2001-2007	**Yale University School of Medicine, Medical Scientist Training Program (MSTP)**, New Haven, CT Doctorate of Medicine, 2005, *cum laude* **Yale University Graduate School of Arts and Sciences, Division of Epidemiology** Doctorate of Philosophy, 2007 Masters of Philosophy, 2005, *distinguished*
2005-2006	**Yale-New Haven Hospital**, New Haven, CT Intern, Department of Internal Medicine
1998-2000	**Yale University School of Public Health, Division of Chronic Disease Epidemiology** Masters in Public Health, 2000
1994-1998	**Rice University**, Houston, TX Bachelor of Arts in Biology and in Sociology, 1998, s*umma cum laude, Phi Beta Kappa*

Honors and Awards

2008	American Society of Clinical Oncology (ASCO) Breast Cancer Symposium Merit Award
2008	M. D. Anderson Cancer Center Odyssey Fellow Award, to support the best postdoctoral trainees among the newest generation of cancer researchers at the institution
2008	Susan G. Komen Houston Affiliate Travel Scholarship, to support participation at the American Society of Clinical Oncology 2008 Breast Cancer Symposium
2006	Original 1st-author paper featured in Nature Clinical Practice Nephrology: **Smith GL**, et al. Arch Intern Med. 2006 May 22;166(10):1134-42.
2005	Comprehensive exams for Ph.D. passed with *distinguished* honors, for achieving the highest possible score in epidemiology, biostatistics, and specialty area exams
2005	American Cancer Society Prize, awarded for the outstanding M.D. thesis in cancer
2005	Farr Scholar, awarded for excellence in research, leadership and creativity in pursuit of medical knowledge as a Yale medical student
2005	Campbell Prize, awarded for the highest score on Step Two of the USMLE for graduating students of Yale University School of Medicine
2005	American Medical Women's Association Glasgow Memorial Achievement Citation, awarded for outstanding women graduates of Yale University School of Medicine
2004-2005	American Heart Association, Kidney in Cardiovascular Disease Council writing committee
2003	Co-Chair for educational session, American College of Cardiology national scientific meeting
1998-2000	Scholarship for academic excellence for Yale School of Epidemiology and Public Health
1998	Phi Beta Kappa
1994	Max Roy scholarship for academic excellence, Rice University
1994	National Merit Scholar
1994	Valedictorian, Quince Orchard High School

Publications & Presentations

Commentaries and Review Article

1. **Smith GL**. Commentary on "Disparities in breast cancer treatment and survival for women with disabilities" McCarthy EP et al. Ann Intern Med 145:637-645, 2006. Breast Diseases Quarterly 2007; 18:211.l

2. **Smith GL,** Buchholz TA. Commentary on "Radiotherapy following breast-conserving surgery for screen-detected ductal carcinoma in situ: indications and utilisation in the UK. Interim findings from the Sloane Project" Dodwell et al. Br J Cancer 97:725-9, 2007. Breast Diseases Quarterly 2008; 19:168.

3. Smith BD, **Smith GL**, Buchhholz TA. Controversies over the role of radiation therapy for ductal carcinoma in situ. Expert Rev Anticancer Ther. 2008 Mar;8(3):433-41.

4. **Smith GL**, Buchholz TA. Commentary on "The use of radiation therapy after breast-conserving surgery in hormonally treated breast cancer patients is dependent on patient age, geographic region, and surgeon specialty" Chagpar et al. Am J Surg 2008 195:793-8. Breast Diseases Quarterly 2009; 19-338-9.

5. **Smith GL,** Buchholz TA. Commentary on "Correlates and Effect of Suboptimal Radiotherapy in Women with Ductal Carcinoma In Situ or Early Invasive Breast Cancer" Gold et al. Cancer 2008 113: 3108-15. Breast Diseases Quarterly 2009; 20:204.

6. **Smith GL**. Commentary on "Completion of Adjuvant Radiation Therapy Among Women With Breast cancer" Srokowski et al. Cancer 2008 113:22-29. Breast Diseases Quarterly 2009; 20:307.

7. **Smith GL.** Commentary on "Population-based study of trends and variations in radiotherapy as part of primary treatment of cancer in the southern Netherlands between 1988 and 2006, with an emphasis on breast and rectal cancer" Vulto et al. Int J Radiat Oncol Biol Phys 2009 74: 464-71. Breast Diseases Quarterly 2009; 20: 439.

Original Manuscripts:

11. **Smith GL**, Shih YT, Giordano SH, Smith BD, Buchholz TA. Predicting breast cancer tumor stage using Medicare claims data. 2009. Epidemiologic Perspectives & Innovations 2010 Jan; 7:1.

12. **Smith GL,** Xu Y, Shih YCT, Giordano SH, Smith BD, Hunt KK, Strom EA, Perkins GH, Hortobagyi GN, Buchholz TA.. Breast-conserving surgery in older patients with invasive breast cancer: Current patterns of treatment across the United States. J Am Coll Surg. 2009 Oct;209(4):425-433. *Highlighted in the Continuing Medical Education (CME) edition.

13. **Smith GL,** Shih YT, Xu Y, Giordano SH, Smith BD, Perkins G, Tereffe W, Woodward WA, Buchholz TA. Racial disparities in treatment for early invasive breast cancer: a national Medicare study of radiotherapy after conservative surgery. Cancer 2010 Feb 1;116(3):734-41.

14. Smith BD, **Smith GL**, Hurria A, Buchholz TA. The future of cancer incidence in the United States: Expected burdens upon an aging, changing nation. J Clin Oncol. 2009 Jun 10;27(17):2758-65.

15. **Smith GL**, Smith BD, Garden AS, Rosenthal DI, Sherman SI, Morrison WH, Schwartz DL, Weber RS, Buchholz TA. Hypothyroidism in older head and neck cancer patients after treatment with radiation: A population-based study. Head and Neck 2009 Aug;31(8):1031-8.

16. Smith BD, **Smith GL**, Roberts KB, Buchholz TA. Baseline utilization of breast radiotherapy prior to institution of the Medicare Practice Quality Reporting Initiative. Int J Radiat Oncol Biol Phys 2009 Aug 1;74(5):1506-12

17. **Smith GL,** Smith BD, Buchholz TA, Liao Z, Jeter M, Swisher SG, Hofstetter WL, Ajani JA, Komaki R, Cox JD. Patterns of care and local-regional treatment outcomes in older esophageal cancer patients. Int J Radiat Oncol Biol Phys. 2009 Jun 1;74(2):482-9

18. **Smith GL**, Smith BD, Buchholz TA, Giordano S, Frank S, Schwartz D, Garden A, Morrison W, Chao C, Woodward WA, Yom S, Weber R, Ang KK, Rosenthal D. Cerebrovascular disease risk in older head and neck cancer patients treated with radiation therapy. J Clin Oncol. 2008 Nov 1;26(31):5119-25. *Highlighted in Cogent Medicine Radiation Oncology, October 2008

19. **Smith GL**, Smith BD, Giordano SH, Shih YC, Woodward WA, Strom EA, Perkins GH, Tereffe W, Yu T, Buchholz TA. Risk of hypothyroidism in older breast cancer patients treated with radiation. Cancer 2008 Mar 15;112(6):1371-9.

20. Smith BD, Haffty BG, **Smith GL**, Hurria A, Buchholz TA, Gross CP. Utilization of Post-Mastectomy Radiation in Older Women. Int J Radiat Oncol Biol Phys 2008 May 1;71(1):98-106.

21. **Smith** GL, Masoudi FA, Shlipak MG, Krumholz HM, Parikh CR. Renal function predicts up to 10-year mortality risks after acute myocardial infarction (AMI) in elderly patients. J Am Soc Nephrol 2008 Jan 19;141-50. Featured in editorial, Feast and famine: Epidemiology and clinical trials in chronic kidney disease. J Am Soc Nephrol 2008 Jan 19; 2-4.

22. Austin B, Wang YF, **Smith GL**, Vaccarino V, Krumholz HM, McNamara R. Systolic function as a predictor of mortality and quality of life in long-term survivors with heart failure. Accepted for publication. Clin Cardiol 2007.

23. Parikh CR, Coca SG, **Smith GL**, Vaccarino V, Krumholz HM. Impact of chronic kidney disease on health-related quality-of-life improvement after coronary artery bypass surgery. Arch Intern Med. 2006 Oct 9;166(18):2014-9.

24. Brosius FC 3rd, Hostetter TH, Kelepouris E, Mitsnefes MM, Moe SM, Moore MA, Pennathur S, **Smith GL**, Wilson PW. Detection of chronic kidney disease in patients with or at increased risk of cardiovascular disease: a science advisory from the American Heart Association Kidney and Cardiovascular Disease Council; the Councils on High Blood Pressure Research, Cardiovascular Disease in the Young, and Epidemiology and Prevention; and the Quality of Care and Outcomes Research Interdisciplinary Working Group: Developed in Collaboration With the National Kidney Foundation. Hypertension. 2006 Oct;48(4):751-5.

25. Brosius FC 3rd, Hostetter TH, Kelepouris E, Mitsnefes MM, Moe SM, Moore MA, Pennathur S, **Smith GL**, Wilson PW. Detection of chronic kidney disease in patients with or at increased risk of cardiovascular disease: a science advisory from the American Heart Association Kidney And Cardiovascular Disease Council; the Councils on High Blood Pressure Research, Cardiovascular Disease in the Young, and Epidemiology and Prevention; and the Quality of Care and Outcomes Research Interdisciplinary Working Group: developed in collaboration with the National Kidney Foundation. Circulation. 2006 Sep 5;114(10):1083-7.

26. Smith BD, Haffty BG, Buchholz TA, **Smith GL**, Galusha DH, Bekelman JE, Gross CP. Effectiveness of radiation therapy in older women with ductal carcinoma in situ. J Natl Cancer Inst. 2006 Sep 20;98(18):1302-10.

27. **Smith GL**, Smith BD, Haffty BG. Rationalization and regionalization of treatment for ductal carcinoma in situ of the breast. Int J Radiat Oncol Biol Phys. 2006 Aug 1;65(5):1397-403.

28. **Smith GL**, Shlipak MG, Havranek EP, Foody JM, Masoudi FA, Rathore SS, Krumholz HM. Serum urea nitrogen, creatinine, and estimators of renal function: mortality in older patients with cardiovascular disease. Arch Intern Med. 2006 May 22;166(10):1134-42.

29. Smith BD, Gross CP, **Smith GL**, Galusha DH, Bekelman JE, Haffty BG. Effectiveness of radiation therapy for older women with early breast cancer. J Natl Cancer Inst. 2006 May 17;98(10):681-90.

30. **Smith GL**, Lichtman JH, Bracken MB, Shlipak MG, Phillips CO, DiCapua P, Krumholz HM. Renal impairment and outcomes in heart failure: systematic review and meta-analysis. J Am Coll Cardiol. 2006 May 16;47(10):1987-96.

31. Kosiborod M, Curtis JP, Wang Y, **Smith GL**, Masoudi FA, Foody JM, Havranek EP, Krumholz HM. Anemia and outcomes in patients with heart failure: a study from the National Heart Care Project. Arch Intern Med. 2005 Oct 24;165(19):2237-44.

32. Cheng S, Lichtman JH, Amatruda JM, **Smith GL**, Mattera JA, Roumanis SA, Krumholz HM. Knowledge of blood pressure levels and targets in patients with coronary artery disease in the USA. J Hum Hypertens. 2005 Oct;19(10):769-74.

33. Smith BD, **Smith GL**, Cooper DL, Wilson LD. The cutaneous B-cell lymphoma prognostic index: a novel prognostic index derived from a population-based registry. J Clin Oncol. 2005 May 20;23(15):3390-5.

34. **Smith GL**, Shlipak MG, Havranek EP, Masoudi FA, McClellan WM, Foody JM, Rathore SS, Krumholz HM. Race and renal impairment in heart failure: mortality in blacks versus whites. Circulation. 2005 Mar 15;111(10):1270-7.

35. Smith BD, **Smith GL**, Haffty BG. Postmastectomy radiation and mortality in women with T1-2 node-positive breast cancer. J Clin Oncol. 2005 Mar 1;23(7):1409-19.

36. Cheng S, Lichtman JH, Amatruda JM, **Smith GL**, Mattera JA, Roumanis SA, Krumholz HM. Knowledge of cholesterol levels and targets in patients with coronary artery disease. Prev Cardiol. 2005 Winter;8(1):11-7.

37. Shlipak MG, **Smith GL**, Rathore SS, Massie BM, Krumholz HM. Renal function, digoxin therapy, and heart failure outcomes: evidence from the digoxin intervention group trial. J Am Soc Nephrol. 2004 Aug;15(8):2195-203.

38. Lichtman JH, Amatruda J, Yaari S, Cheng S, **Smith GL**, Mattera JA, Roumanis SA, Wang Y, Radford MJ, Krumholz HM. Clinical trial of an educational intervention to achieve recommended cholesterol levels in patients with coronary artery disease. Am Heart J. 2004 Mar;147(3):522-8.

39. Smith BD, Glusac EJ, McNiff JM, **Smith GL**, Heald PW, Cooper DL, Wilson LD. Primary cutaneous B-cell lymphoma treated with radiotherapy: a comparison of the European Organization for Research and Treatment of Cancer and the WHO classification systems. J Clin Oncol. 2004 Feb 15;22(4):634-9.

40. Rathore SS, Foody JM, Wang Y, **Smith GL**, Herrin J, Masoudi FA, Wolfe P, Havranek EP, Ordin DL, Krumholz HM. Race, quality of care, and outcomes of elderly patients hospitalized with heart failure. JAMA. 2003 May 21;289(19):2517-24.

41. **Smith GL**, Masoudi FA, Vaccarino V, Radford MJ, Krumholz HM. Outcomes in heart failure patients with preserved ejection fraction: mortality, readmission, and functional decline. J Am Coll Cardiol. 2003 May 7;41(9):1510-8.

42. **Smith GL,** Vaccarino V, Kosiborod M, Lichtman JH, Cheng S, Watnick SG, Krumholz HM. Worsening renal function: what is a clinically meaningful change in creatinine during hospitalization with heart failure? J Card Fail. 2003 Feb;9(1):13-25.

43. Kosiborod M, **Smith GL**, Radford MJ, Foody JM, Krumholz HM. The prognostic importance of anemia in patients with heart failure. Am J Med. 2003 Feb 1;114(2):112-9.

44. Krumholz HM, Amatruda J, **Smith GL,** Mattera JA, Roumanis SA, Radford MJ, Crombie P, Vaccarino V. Randomized trial of an education and support intervention to prevent readmission of patients with heart failure. J Am Coll Cardiol. 2002 Jan 2;39(1):83-9.

45. Havranek EP, Masoudi FA, **Smith GL**, Wolfe P, Ralston DL, Krumholz HM, Ordin DL. Lessons learned from the national heart failure project: a Center for Medicare and Medicaid services initiative to improve the care of Medicare beneficiaries with heart failure. Congest Heart Fail. 2001 Nov;7(6):334-336.

46. Wexler DJ, Chen J, **Smith GL**, Radford MJ, Yaari S, Bradford WD, Krumholz HM. Predictors of costs of caring for elderly patients discharged with heart failure. Am Heart J. 2001 Aug;142(2):350-7.

47. Smith BD, **Smith GL**, Carter D, DiGiovanna MP, Kasowitz KM, Sasaki CT, Haffty BG. Molecular marker expression in oral and oropharyngeal squamous cell carcinoma. Arch Otolaryngol Head Neck Surg. 2001 Jul;127(7):780-5.

48. Smith BD, **Smith** GL, Carter D, Sasaki CT, Haffty BG. Prognostic significance of vascular endothelial growth factor protein levels in oral and oropharyngeal squamous cell carcinoma. J Clin Oncol. 2000 May;18(10):2046-52.

In Progress

1. **Smith GL**, Shih YT, Xu Y, Giordano SH, Smith BD, Buchholz TA. Breast brachytherapy in the United States: How is this emerging modality being incorporated into the care of older breast cancer patients? 2009. Under review at J Clin Oncol.

Abstracts and Presentations at National Scientific Meetings:

1. **Smith GL**, Xu Y, Buchholz TA, Smith BD, Giordano SH, Shih YCT. Breast brachytherapy in the United States: utilization patterns in older patients after breast-conserving surgery. Abstract 2009. (Oral presentation: American Society of Therapeutic Radiology and Oncology).

2. **Smith GL**, Shih YT, Xu Y, Giordano SH, Smith BD, Buchholz TA. Breast brachytherapy in the United States: How is this emerging modality being incorporated into the care of older breast cancer patients? Abstract 2008. (Poster presentation: San Antonio Breast Cancer Symposium)

3. **Smith GL**, Shih YT, Xu Y, Giordano SH, Smith BD, Perkins GH, Tereffe W, Woodward WA, Buchholz TA. Racial disparities in treatment for early invasive breast cancer: A national Medicare study of radiotherapy after conservative surgery. Abstract 2008. (Poster presentation: American Society of Clinical Oncology 2008 Breast Cancer Symposium). Highlighted by Medscape Oncology, Reuters, Healthday news, Houston Chronicle, and Houston public radio.

4. **Smith GL**, Smith BD, Giordano SH, Shih YC, Woodward WA, Strom EA, Perkins GH, Oh JL, Tereffe W, Buchholz TA. Risk of hypothyroidism in older breast cancer patients treated with radiotherapy. Abstract 2007 (Poster presentation: American Society for Therapeutic Radiology and Oncology)

5. Roberts KB, Van Hoff J, **Smith GL**, Gurney JG, Kadan-Lottick NS. Radiotherapy for childhood gliomas: possible detriment in long term survival. Abstract 2007 (Poster presentation: American Radium Society).

6. **Smith GL**, Smith BD, Haffty BG. Trends and variation in radiotherapy use for ductal carcinoma in situ (DCIS): achieving a minimal standard. International Journal of Radiation Oncology, Biology, and Physics 60(1) Suppl: S209-10, 2004. (Oral presentation: American Society of Therapeutic Radiology and Oncology)

7. **Smith GL**, Lichtman JH, Krumholz HM. Functional status and quality of life in heart failure patients with renal impairment. Circulation 106(16):e76, 2002 (Abstract).

8. **Smith GL**, Vaccarino V, Kosiborod M, Lichtman JH, Cheng S, Krumholz HM. Worsening renal function: What is a clinically meaningful change in creatinine during hospitalization with heart failure? Journal of the American College of Cardiology 39 (5) Suppl A: Abstract 890-2, 2002. (Abstract) (Oral presentation: Annual meeting for the American College of Cardiology)

9. **Smith GL**, Radford MJ, Rathore SS, Lichtman JH, Watnick SG, Krumholz HM. Elevated serum creatinine and increased mortality in women and elderly heart failure patients. Journal of the American College of Cardiology 39 (5) Suppl A: Abstract 1098-170, 2002 Mar. (Abstract)

10. **Smith GL**, Havranek EP, Masoudi FA, Wolfe P, Ordin DL, Krumholz HM. Sex and heart failure with preserved systolic function. Journal of Cardiac Failure 7(3) Suppl 1:68, 2001. (Abstract)

11. **Smith GL**, Havranek EP, Masoudi FA, Wolfe P, Ordin DL, Krumholz HM. Sex differences in quality of care for patients with heart failure. Journal of Cardiac Failure 7(3) Suppl 1:76, 2001. (Abstract)

Theses

1. Ph.D.: **Smith GL.** Renal Impairment in Heart Failure: Prevalence, Prognosis, and Detection. 2007.
2. M.D.: **Smith GL.** Patterns of Treatment for Ductal Carcinoma in Situ of the Breast: Rationale for a Minimal Standard. 2005.
3. M.P.H.: **Smith GL**. Social Contact and Hospital Costs in Heart Failure Patients. 2000.
4. B.A. Honors: **Li G**. Race and Resource Utilization by Victims of Domestic Violence: the Houston Area Women's Center. 1998.

Grant Funding

1. Multidisciplinary Postdoctoral Award, Department of Defense Congressionally Directed Medical Research Programs, 2006 Breast Cancer Research Program. Term: July 2007-June 2010. Amount: $692,344. Project title: Patterns of care and disparities in the treatment of early breast cancer.
2. Odyssey Fellow Award, M. D. Anderson Cancer Center. Term: September 2008-September 2010. Project title: Patterns of care for older breast cancer patients.

Certification

11/2006	United States Medical Licensing Examination, Step III, 99 of 99
1/2005	United States Medical Licensing Examination, Step II-Clinical Skills, *pass*
7/2004	United States Medical Licensing Examination, Step II-Clinical Knowledge, 99 of 99
6/2003	United States Medical Licensing Examination, Step I, 99 of 99

Peer Reviewer

International Journal of Radiation Oncology, Biology, and Physics
Clinical Therapeutics
Cancer

Teaching

2002-2003	Teaching Fellow, Cell Biology and Histology, Yale University School of Medicine
2000	Teaching Fellow, Data Management and Analysis, Yale University School of Public Health

Mentorship

June 2008- August 2008 Anna Zamarripa, The University of Texas M. D. Anderson Cancer Center Summer Intern Program

Original Article

Racial Disparities in the Use of Radiotherapy After Breast-Conserving Surgery

A National Medicare Study

Grace L. Smith, MD, PhD, MPH[1]; Ya-Chen T. Shih, PhD[2]; Ying Xu, MD, MS[2]; Sharon H. Giordano, MD, MPH[3]; Benjamin D. Smith, MD[1,4]; George H. Perkins, MD[1]; Welela Tereffe, MD[1]; Wendy A. Woodward, MD, PhD[1]; and Thomas A. Buchholz, MD[1]

BACKGROUND: In prior studies, the use of standard breast cancer treatments has varied by race, but previous analyses were not nationally representative. Therefore, in a comprehensive, national cohort of Medicare patients, racial disparities in the use of radiotherapy (RT) after breast-conserving surgery (BCS) for invasive breast cancer were quantified. **METHODS:** A national Medicare database was used to identify all beneficiaries (age >65 years) treated with BCS for incident invasive breast cancer in 2003. Claims codes identified RT use, and Medicare demographic data indicated race. Logistic regression modeled RT use in white, black, and other-race patients, adjusted for demographic, clinical, and socioeconomic covariates. **RESULTS:** Of 34,080 women, 91% were white, 6% were black, and 3% were another race. The mean age of the patients was 76 ± 7 years. Approximately 74% of whites, 65% of blacks, and 66% of other-race patients received RT ($P < .001$). After covariate adjustment, whites were found to be significantly more likely to receive RT than blacks (odds ratio, 1.48; 95% confidence interval, 1.34-1.63 [$P < .001$]). Disparities between white and black patients varied by geographic region, with blacks in areas of the northeastern and southern United States demonstrating the lowest rates of RT use (57% in these regions). In patients age <70 years, racial disparities persisted. Specifically, 83% of whites, 73% of blacks, and 78% of other races in this younger group received RT ($P < .001$). **CONCLUSIONS:** In this comprehensive national sample of older breast cancer patients, substantial racial disparities were identified in RT use after BCS across much of the United States. Efforts to improve breast cancer care require overcoming these disparities, which exist on a national scale. ***Cancer*** **2010;116:734–41.** © *2009 American Cancer Society.*

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Postoperative radiotherapy (RT) is generally considered a standard component of therapy for patients diagnosed with early invasive breast cancer who undergo breast-conserving surgery (BCS). Cumulative results from randomized trials have demonstrated local control and survival benefits with the addition of RT after BCS.[1-4] However, despite the evidence supporting the use of RT after BCS, a recent analysis of treatment patterns in breast cancer patients enrolled in the North American Fareston versus Tamoxifen Adjuvant (NAFTA) trial suggested that racial disparities may exist in RT use after BCS. Specifically, this study found that postoperative RT was administered in 82% of white patients but only 70% of black patients, although the difference was not found to be statistically significant.[5]

Other studies of breast cancer patients have also suggested racial disparities in the receipt of standard treatments for locally advanced and regional disease, including differences among white and nonwhite patients in the use of RT, surgery, and chemotherapy.[5-15] Results from many of these studies suggest that nonwhite patients may more frequently encounter

Corresponding author: Thomas A. Buchholz, MD, Department of Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Unit 97, Houston, TX 77030; Fax: (713) 563-6940; tbuchhol@mdanderson.org.

[1]Department of Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, Texas; [2]Section of Health Services Research, Department of Biostatistics, The University of Texas M. D. Anderson Cancer Center, Houston, Texas; [3]Department of Breast Medical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, Texas; [4]Radiation Oncology Flight, Wilford Hall Medical Center, Lackland Air Force Base, Texas

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barriers to receiving standard care. However, prior analyses were conducted on limited samples, including single-state, single-center, or clinical trial patient cohorts, and studies of population-based cohorts have not to our knowledge been nationally comprehensive. Consequently, the true magnitude of and regional variation in racial disparities in breast cancer treatment across the United States remain uncertain.

Quantifying the magnitude of racial disparities in the use of standard treatments across the nation is an important step toward identifying and ultimately reducing barriers to high-quality breast cancer care. Therefore, using data from a comprehensive, national sample of Medicare patients, we sought to quantify racial differences in the use of RT after BCS for women with invasive breast cancer. In addition, we sought to determine whether there was geographic variation across the United States in the association between race and RT use.

MATERIALS AND METHODS

National Medicare Data Set and Study Sample Derivation

The national Medicare data set includes comprehensive claims data for all Medicare beneficiaries in the United States. Files contain data collected by Medicare for reimbursement of healthcare services for each beneficiary and include institutional (inpatient and outpatient) and non-institutional (physicians or other providers) final action claims.[16] The University of Texas M. D. Anderson Cancer Center's institutional review board approved use of the Medicare database for this study.

We used the following algorithm to identify patients with incident breast cancer, which we based on a prior validated algorithm using claims data.[17,18] Our initial study population was comprised of 853,273 women who had any diagnosis of invasive breast cancer in 2003, defined as an International Classification of Diseases-Ninth Revision (ICD-9) diagnosis code of 174. Because this denominator would have included incident and prevalent cases in 2003, as well as potentially disease-free patients undergoing breast cancer screening, we applied the following algorithm to refine our study sample to identify incident cases only. From our initial study population, we included 83,611 patients aged $\geq$65 years who underwent BCS between January 1, 2003, and December 31, 2003. From this sample, we excluded 17,872 patients who did not have at least 2 claims (on different dates) specifying a diagnosis of invasive breast cancer between January 1, 2003, and December 31, 2004 (at least 1 claim must have occurred during 2003), with no more than 6 months between the date of BCS and the earliest breast cancer diagnosis claim date. To exclude the prevalent cases, we excluded 10,362 patients who had a breast cancer-related diagnosis or procedure claim between January 1, 2002, and December 31, 2002. To ensure that BCS was intended to be the primary cancer-directed surgery, we excluded 13,470 patients who underwent mastectomy within 3 months of BCS. To limit our sample to patients with early stage invasive breast cancer, we then excluded 1082 patients who had $\geq$2 claims specifying metastatic breast cancer from 3 months before to 3 months after the diagnosis date. To improve sample homogeneity, we also excluded 2964 patients who were receiving Medicare coverage because of end-stage renal disease or disability. Finally, to ensure we had complete claims information to determine patients' cancer treatment course and comorbidities, we excluded 3781 patients who lacked Medicare Part A or B coverage or who had intermittent health maintenance organization coverage in the 9 months after or in the 1 year before their breast cancer diagnosis date (of these patients, 2143 had incomplete information in the year before diagnosis because they were aged $<$66 years). For our study, the breast cancer diagnosis date was considered the date of the earliest claim for a diagnosis of breast cancer. This left a final sample size of 34,080 patients. The complete list of claims codes applied in our algorithm can be found in Table 1.

RT and Race

Patients were considered to have received breast RT if a claim for RT (Appendix A) occurred within 9 months of the breast cancer diagnosis date. This definition has been validated in prior studies of breast cancer patients.[19-24] In addition, for patients classified as receiving RT, completion of the therapeutic course was defined as at least 3 complete weeks of therapy (5 treatments per week). Patient race was determined using the Medicare denominator file, which contains demographic information on each beneficiary. In this file, race and ethnicity data are based on the patients' self-report. For our analysis, we categorized patients as white, black, and other (nonwhite, nonblack) race based on a prior study of the sensitivity and specificity of Medicare race and ethnicity groupings.[25]

Other Covariates

Demographic and clinical covariates were derived from Medicare files, including the denominator file and claims files. Demographic data included age at diagnosis and

Table 1. Claims Codes

Variable	ICD-9 Code	CPT Code
Breast-conserving surgery	85.20, 85.21, 85.22, 85.23	19120, 19125, 19126, 19160, 19162
Breast cancer-related diagnosis and procedure claims		
Biopsy	85.1-85.19	19000, 19001, 19100, 19101, 19110, 19112
Breast-conserving surgery	As above	As above
Mastectomy	85.33-85.48	19180-19255
Lymph node dissection	40.3	38525, 38740, 38745
Radiotherapy	92.2-92.29, 0330*, 0333*	77400-77499, 77520-77525, 77750-77799
History of breast cancer	V10.3	—

ICD-9 indicates International Classification of Diseases, Ninth Revision; CPT, Current Procedural Terminology.
*Revenue Center code.

state of residence, with geographic regions based on the Census Divisions.[26] Disease-related and treatment-related variables included axillary lymph node involvement; axillary lymph node dissection; sentinel lymph node biopsy; receipt of any chemotherapy; receipt of doxorubicin or paclitaxel; any staging imaging; number of hospitalizations in the year after diagnosis; and number of medical oncology, radiation oncology, and surgery visits in the year after diagnosis. Variables indicating preventive healthcare and interactions with the healthcare system included mammography in the year before diagnosis and number of physician visits in the year before diagnosis. In addition, we calculated the severity of comorbid disease for each patient based on a modified Charlson comorbidity score validated in a prior claims-based study: 0 (no comorbidity), 1 (mild to moderate), or $\geq$2 (severe).[27] This score combined comorbidities recorded in Medicare claims during the 12 months before the patient's cancer diagnosis. To enhance the specificity of comorbid disease diagnoses, patients must have had at least 1 inpatient (Part A) claim or at least 2 outpatient (Part B) claims more than 30 days apart.[27] Socioeconomic covariates were derived from the 2003 Area Resource File[28] linked to the Medicare files by county and state, and included rural/urban status, percentage of population (by county) living in poverty, median income, education level, density of surgeons, and density of radiation oncologists.

Statistical Analysis

All analyses were conducted using SAS software (version 9.1.3; SAS Institute Inc, Cary, NC), and all statistical tests assumed a 2-tailed α of 0.05. We calculated percentage RT use for the entire sample, by state and by region, and tested the unadjusted association between receipt of RT and race using the Pearson chi-square test. Bivariate associations between receipt of RT and other covariates were tested using the Pearson chi-square test for categoric variables and the Wilcoxon rank sum test for continuous variables. A multivariate logistic model tested the adjusted association between receipt of RT and race. Covariates were selected a priori based on significance in bivariate analyses ($P < .25$) and significance in prior studies of cancer patients.[19-24] Goodness of fit was assessed using the Hosmer and Lemeshow test. The final parsimonious multivariate logistic model was then also used to calculate adjusted rates of RT use.[29] A subsidiary model included socioeconomic covariates and tested the association in the subset of 33,172 patients who had socioeconomic covariate data available.

We further examined the association between receipt of RT and race in the subset of patients age <70 years (n = 7270), because prior evidence has suggested that the use of RT after BCS is more common in younger patients.[5] In sensitivity analyses, we tested the association between race and receipt of RT in the subset of patients with a more restrictive (specific) definition of invasive breast cancer, which required the 2 diagnosis codes for invasive breast cancer to be $\geq$30 days apart (n = 33,114), and in a more restrictive definition of breast cancer, which excluded patients with any diagnosis code of ductal carcinoma in situ (DCIS) (ICD-9 diagnosis code 233.0) within 6 months of the invasive breast cancer diagnosis date (n = 22,301). We also tested a less restrictive treatment window of RT within 12 months of breast cancer diagnosis to take into account possible racial differences in treatment delays. Finally, in patients (of any age) who received RT, we also examined the association between completion of RT course and race.

RESULTS

Patient Characteristics

Of the 34,080 women with invasive breast cancer who were treated with BCS, 91% (N = 31,127) were white,

6% (N = 2077) were black, and 3% (N = 876) were another race. The mean age of the sample was 76 (standard deviation, 7) years. Approximately 73% of patients received RT after BCS, and 13% received chemotherapy as part of their initial treatment course. Approxmately 39% of patients had a claim indicating axillary lymph node dissection or axillary lymph node involvement, and 55% had a claim indicating sentinel lymph node biopsy (Table 2).

Table 2. Sample Characteristics

Characteristic	Percentage
Demographic	
Mean age (SD), y	76 (7)
Race	
White	91
Black	6
Other	3
Region	
West, Pacific West	11
West, Mountain West	5
Midwest, West North Central	7
Midwest, East North Central	19
Northeast, New England	7
Northeast, Mid-Atlantic	16
South, South Atlantic	21
South, West South Central	9
South, East South Central	5
Not known	1
Clinical	
No comorbid diseases	32
Axillary lymph node involvement	39
Sentinel lymph node biopsy	55
Radiotherapy	73
Chemotherapy	13
Socioeconomic	
Mean income (SD), $US	43,429 (10,649)
Education	
Mean percent completed less than ninth grade (SD)	7 (4)
Mean percent completed college or higher (SD)	24 (9)
Mean surgeon density (per 100,000) (SD)	13 (10)
Mean radiation oncologist density (per 100,000) (SD)	1.5 (1.4)

SD indicates standard deviation.

Race and RT Use

Significant racial differences were found to exist in the receipt of RT; 74% of white women, 65% of black women, and 66% of other-race women received RT after BCS ($P < .001$). After adjustment for demographic, clinical, and socioeconomic covariates, white women were still significantly more likely than black women to have received RT after BCS (odds ratio [OR], 1.48; 95% confidence interval [95% CI], 1.34-1.63 [$P < .001$]). In addition, there was a trend toward white women also being more likely than other-race women to have received RT after BCS (OR, 1.22; 95% CI, 1.04-1.42 [$P = .01$]) (Table 3). Other variables found to be independently associated with higher rates of RT use included geographic region, younger age, lower comorbidity score, treatment with doxorubicin, axillary lymph node dissection, use of staging imaging, use of mammography before cancer diagnosis, and greater number of physician visits (interactions with the healthcare system) in the year before cancer diagnosis. In the subset of patients with complete socioeconomic covariate data available, the association between receipt of RT and race was unchanged. In this model, lower poverty level, higher median income, higher education level, higher surgeon density, and higher radiation oncologist density were also found to be associated with receipt of RT.

Sensitivity analyses using more restrictive definitions of invasive breast cancer did not appear to alter the magnitude or significance of the associations between race and RT use significantly. Sensitivity analyses using a less restrictive treatment window also did not appear to alter the magnitude or significance of these associations.

In the subset of patients age <70 years, 82% received RT after BCS. Specifically, 83% of white women, 73% of black women, and 78% of other-race women received RT after BCS ($P < .001$). On multivariate analysis of this younger group, white women were still found to be significantly more likely than black women to have received RT after BCS (OR, 1.73; 95% CI, 1.40-2.14 [$P = .003$]), although there was no significant difference noted between white women and other-race women (OR, 1.28; 95% CI, 0.86-1.90 [$P = .22$]). The interaction term between race (black vs white race) and age (age <70 years vs ≥70 years) was not found to be statistically significant ($P = .19$).

In the subset of patients who received RT and had the number of treatments documented, 85% were found to have completed a course of therapy, whereas 15% had an incomplete course. Approximately 85% of white women, 85% of black women, and 82% of other-race women completed their RT course ($P = .02$). After adjusting for covariates, there remained no significant difference in rates of completion by race (black vs white women: OR, 1.00; 95% CI, 0.83-1.20 [$P = .99$] and other-race vs white women: OR, 1.02; 95% CI, 0.73-1.43 [$P = .89$]).

Table 3. Racial Disparities in the Use of Radiotherapy After Breast-Conserving Surgery for Breast Cancer

Model: RT use	OR	95% CI	*P*
Unadjusted			
White vs black patients	1.52	1.38-167	<.001
White vs other* patients	1.46	1.27-1.68	<.001
Adjusted†			
White vs black patients	1.48	1.34-1.63	<.001
White vs other* patients	1.22	1.04-1.42	.01

*RT indicates radiotherapy; OR, odds ratio; 95% CI, 95% confidence interval.

†Adjusted for age, comorbidity, chemotherapy (doxorubicin or paclitaxel), axillary lymph node involvement, staging, imaging, surgeon visits, mammography, physician visits, and region.

Geographic Variation in Racial Disparities

We observed significant geographic variations in racial disparities. The absolute difference in the percentage of RT use between white and black women by state ranged from −28% to 74%. However, for most states, the percentage of white women who received RT was greater than the percentage of black women who received RT, and in no state was the rate of RT use found to be significantly greater in black women compared with white women (Fig. 1). In areas of the northeastern and southern United States, the racial disparity between white and black women with regard to RT use was particularly pronounced (Fig. 2) (Table 4). Our data were insufficient to assess variations by state or region for other-race women.

DISCUSSION

In our analysis of a national sample of US women aged ≥65 years who were diagnosed with invasive breast cancer, white women (74%) were significantly more likely than black women (65%) to receive RT after BCS. The results of the current study also suggested that white patients were also more likely than patients of other races (66%) to receive RT after BCS. Furthermore, even after we took into consideration other covariates such as patient comorbidity, white women were still nearly 50% more likely than black women to receive RT. The racial disparity between whites and blacks persisted even among the younger patients in the cohort, those age <70 years, in whom RT after BCS was more common. Our analysis also identified geographic variations in the magnitude of treatment disparities between white and black patients across the United States, although some degree of treatment disparity existed in most states. Furthermore, the disparities across the nation persisted even after adjusting for variations in socioeconomic factors such as income, education, and access to healthcare resources. The large magnitude of racial disparities in RT use identified in the current study is concerning given that the administration of RT after BCS in patients with early invasive breast cancer reduces the risk of disease recurrence and breast cancer-related death and is considered the standard of care.[1-4,30]

Other studies have also described disparities in breast cancer care between black patients and white patients.[15] In a recent secondary analysis of the NAFTA trial, in which all patients in the study cohort were treated with BCS and hormonal therapy, 80% of all enrollees received RT. Similar to the 9% to 10% absolute difference noted in the current study, there was a 12% absolute difference found between white and black patients in the rate of RT use in the NAFTA study.[5] A recent analysis of the Surveillance, Epidemiology, and End Results (SEER)-Medicare cohort reported an 8% absolute difference between white and black patients with regard to the receipt of RT after BCS, with 86% of white women and 78% of black women between the ages of 66 and 85 years with invasive breast cancer receiving the treatment.[31] A limitation of this study was that SEER-Medicare sampled ≤ 26% of the US Medicare population, compared with the current study, which sampled the Medicare population in its entirety.

A previous study of breast cancer patients who were treated in the state of Florida found that Hispanic women were significantly less likely to receive local therapy for breast cancer than non-Hispanic white women,[14] whereas another study of patients in Hawaii found that Asian women may be less likely to receive therapy than white women.[32] In our cross-sectional study, we were unable to explore the use of RT in specific nonwhite, nonblack ethnic groups because of the limited sample size of each ethnic group in our sample. Future analyses may seek to focus on exploring national patterns in potential treatment disparities affecting women of other racial/ethnic groups.

The underlying reasons for the racial disparities observed in the current study cohort remain to be determined.[33] Prior studies have identified access to care and socioeconomic factors (such as the patients' income and education, the cost of RT, or the availability of supplemental insurance) as factors that may influence racial disparities in cancer care,[34,35] but even after adjustment for markers of healthcare access in the current analysis, such as number of physician visits and use of mammography before cancer diagnosis, racial disparities persisted. Other

unmeasured potential explanatory factors include the impact of the physician-patient interaction.[36] For example, it is not known whether physicians offer treatment less frequently to nonwhite patients, whether substandard care occurs more frequently in predominantly nonwhite communities, or whether nonwhite patients are more likely to decline treatment. Additional social factors, such as culturally specific health beliefs, the presence of social support, and marital status,[37] also could affect racial disparities in care and may be important variables to explore in future studies seeking to identify specific barriers in breast cancer care.

The underlying causes of the geographic variations in racial disparities also require further study. Several published analyses have indicated that geographic variations in breast cancer care exist,[7,8,38] but to the best of our knowledge no prior study has described how geographic patterns in care may be modified by patient race. Our analysis found that disparities between white and black

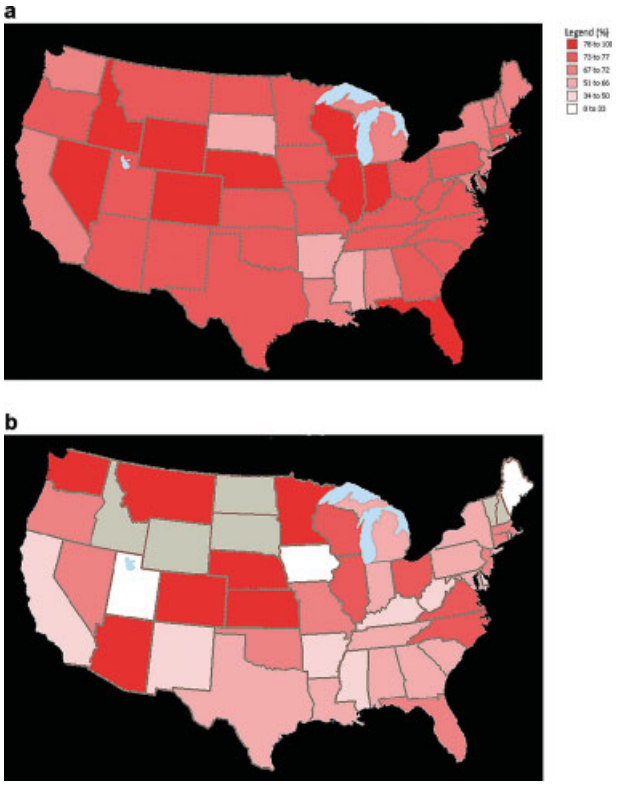

Figure 1. Percentage radiotherapy use in (a) white patients versus (b) black patients is shown. Gray shading indicates that the sample size was too small to provide meaningful data.

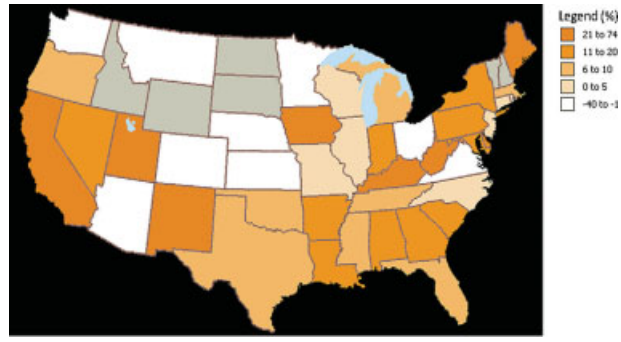

Figure 2. Absolute difference in the rate of radiotherapy (RT) use between white and black patients is shown. An absolute difference <0% indicates that the percentage of black women receiving RT was greater than the percentage of white women. Gray shading indicates that the sample size was too small to provide meaningful data.

Table 4. Unadjusted and Adjusted Regional Variations in the Rate of Radiotherapy Usage Between White and Black Patients With Breast Cancer

		Unadjusted			Adjusted*		
Region	States	% Whites	% Blacks	*P*	% Whites	% Blacks	*P*
West, Pacific West	AK, CA, HI, OR, WA	72	54	<.001	74	61	.07
West, Mountain West	AZ, CO, ID, MT, NV, NM, UT, WY	77	78	.88	72	67	.59
Midwest, West North Central	IA, KS, MN, MO, NE, ND, SD	74	73	.94	74	70	.67
Midwest, East North Central	IL, IN, MI, OH, WI	76	72	.04	79	73	.15
Northeast, New England	CT, MA, NH, ME, RI, VT	72	69	.53	78	71	<.001
Northeast, Mid-Atlantic	NJ, NY, PA	71	57	<.001	70	62	.01
South, South Atlantic	DE, DC, FL, GA, MD, NC, SC, VA, WV	76	68	<.001	73	64	.009
South, West South Central	AR, LA, OK, TX	74	63	.001	69	59	<.001
South, East South Central	AL, KY, MS, TN	72	57	<.001	78	60	.001

*Adjusted for all covariates except state/region.

patients in RT after BCS appeared most pronounced in the northeastern and southern regions of the United States. Given that racial disparities do not appear to be concentrated in a single area of the country, the underlying reasons for disparities in the different regions of the United States are likely to be varied, complex, and multifactorial. For example, rural/urban differences may play a role in the geographic variations in treatment disparities. Prior studies have identified patients' distance from RT facilities as a potential barrier to treatment,[12,39] and suggested that patients living in rural areas may have less access to RT.[39,40] However, a recent study reported similar rates of RT use after mastectomy and after lumpectomy in urban versus rural locales.[41] The study's results suggest that disadvantaged patients in either setting may experience distinct but persistent treatment barriers. Prospective efforts to overcome disparities in cancer treatment, such as the Patient Navigation program,[42] are currently being evaluated and may serve as an important source for identifying the key barriers to cancer care in different geographic regions of the United States.

The current study has limitations to consider. Our sample focused on older breast cancer patients with continuous fee-for-service Medicare Parts A and B insurance coverage. Therefore, future studies will be required to validate the magnitude and significance of racial disparities in the treatment of younger patients. In addition, studies are also needed to determine the magnitude of racial disparities among patients with other insurance status, such as those with Medicaid, given that prior evidence suggests that patients with Medicare insurance coverage are actually more likely to receive appropriate breast cancer treatment.[43] Furthermore, our definitions of invasive breast cancer and RT were claims-based and, therefore, may be subject to misclassification bias. However, the results of the current study demonstrated reproducibility, even after applying the more restrictive criteria to exclude potential metastatic disease and DCIS. Prior studies indicate a high degree of validity for claims-based treatment variables and suggest that, although our treatment definition was unlikely to be 100% sensitive, our percentage use may underestimate true use rates by only approximately 2%.[37] Finally, the racial distribution of patients in the current study sample differs from the general population distribution. Notably, 6% of our sample was black, whereas 9% of US women (age >65 years) are black.[26] This difference is likely due to the tendency of nonwhite patients to receive mastectomy over BCS even for the treatment of early stage disease.[44-46]

Conclusions

To the best of our knowledge, the current study provides 1 of the first available data sets describing a quality indicator for breast cancer care across a comprehensive national sample of older breast cancer patients and was able to identify substantial racial disparities in care across the United States. Our analysis helps define the scope of the treatment disparities in RT after BCS and underscores the concern that this treatment disparity occurs not merely in isolation but is instead a problem that exists on a national scale. Future efforts to improve breast cancer care will require identifying and overcoming the underlying causes of these racial disparities. As additional data become available, future studies may also explore changes in the magnitude of disparities over time and the effect of these disparities in care on breast cancer outcomes.

CONFLICT OF INTEREST DISCLOSURES

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REFERENCES

1. Clarke M, Collins R, Darby S, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. *Lancet*. 2005;366:2087-2106.
2. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med*. 2002;347:1233-1241.
3. Jatoi I, Proschan MA. Randomized trials of breast-conserving therapy versus mastectomy for primary breast cancer: a pooled analysis of updated results. *Am J Clin Oncol*. 2005;28:289-294.
4. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med*. 2002;347:1227-1232.
5. Chagpar AB, McMasters KM, Scoggins CR, Martin RC Jr, Thoene C, Edwards MJ. The use of radiation therapy after breast-conserving surgery in hormonally treated breast cancer patients is dependent on patient age, geographic region, and surgeon specialty. *Am J Surg*. 2008;195:793-798.
6. Ballard-Barbash R, Potosky AL, Harlan LC, Nayfield SG, Kessler LG. Factors associated with surgical and radiation therapy for early stage breast cancer in older women. *J Natl Cancer Inst*. 1996;88:716-726.
7. Baxter NN, Virnig BA, Durham SB, Tuttle TM. Trends in the treatment of ductal carcinoma in situ of the breast. *J Natl Cancer Inst*. 2004;96:443-448.
8. Buchholz TA, Theriault RL, Niland JC, et al. The use of radiation as a component of breast conservation therapy in National Comprehensive Cancer Network Centers. *J Clin Oncol*. 2006;24:361-369.

9. Gold HT, Dick AW. Variations in treatment for ductal carcinoma in situ in elderly women. *Med Care*. 2004;42: 267-275.
10. Griggs JJ, Culakova E, Sorbero ME, et al. Effect of patient socioeconomic status and body mass index on the quality of breast cancer adjuvant chemotherapy. *J Clin Oncol*. 2007;25:277-284.
11. Katz SJ, Lantz PM, Janz NK, et al. Patterns and correlates of local therapy for women with ductal carcinoma-in-situ. *J Clin Oncol*. 2005;23:3001-3007.
12. Punglia RS, Weeks JC, Neville BA, Earle CC. Radiation therapy after mastectomy between 1991 and 1999 in elderly women: response to clinical trial information. *J Clin Oncol*. 2006;24:3474-3482.
13. Richardson LC, Tian L, Voti L, et al. The roles of teaching hospitals, insurance status, and race/ethnicity in receipt of adjuvant therapy for regional-stage breast cancer in Florida. *Am J Public Health*. 2006;96:160-166.
14. Voti L, Richardson LC, Reis I, Fleming LE, Mackinnon J, Coebergh JW. The effect of race/ethnicity and insurance in the administration of standard therapy for local breast cancer in Florida. *Breast Cancer Res Treat*. 2006;95:89-95.
15. Freedman RA, He Y, Winer EP, Keating NL. Trends in racial and age disparities in definitive local therapy of early-stage breast cancer. *J Clin Oncol*. 2009;27:713-719.
16. Research Data Assistance Center Medicare Data File Descriptions. Available at: http://www.resdac.umn.edu/Medicare Accessed December 2008.
17. Nattinger AB, Laud PW, Bajorunaite R, Sparapani RA, Freeman JL. An algorithm for the use of Medicare claims data to identify women with incident breast cancer. *Health Serv Res*. 2004;39:1733-1749.
18. Gold HT, Do HT. Evaluation of three algorithms to identify incident breast cancer in Medicare claims data. *Health Serv Res*. 2007;42:2056-2069.
19. Smith BD, Gross CP, Smith GL, Galusha DH, Bekelman JE, Haffty BG. Effectiveness of radiation therapy for older women with early breast cancer. *J Natl Cancer Inst*. 2006;98:681-690.
20. Smith BD, Haffty BG, Buchholz TA, et al. Effectiveness of radiation therapy in older women with ductal carcinoma in situ. *J Natl Cancer Inst*. 2006;98:1302-1310.
21. Smith BD, Haffty BG, Smith GL, Hurria A, Buchholz TA, Gross CP. Use of postmastectomy radiotherapy in older women. *Int J Radiat Oncol Biol Phys*. 2008;71:98-106.
22. Smith BD, Smith GL, Buchholz TA. Controversies over the role of radiation therapy for ductal carcinoma in situ. *Expert Rev Anticancer Ther*. 2008;8:433-441.
23. Smith BD, Smith GL, Haffty BG. Postmastectomy radiation and mortality in women with T1-2 node-positive breast cancer. *J Clin Oncol*. 2005;23:1409-1419.
24. Smith GL, Smith BD, Giordano SH, et al. Risk of hypothyroidism in older breast cancer patients treated with radiation. *Cancer*. 2008;112:1371-1379.
25. Arday SL, Arday DR, Monroe S, Zhang J. HCFA's racial and ethnic data: current accuracy and recent improvements. *Health Care Financ Rev*. 2000;21:107-116.
26. US Census Bureau. Available at: http://www.census.gov Accessed December 2008.
27. Klabunde CN, Potosky AL, Legler JM, Warren JL. Development of a comorbidity index using physician claims data. *J Clin Epidemiol*. 2000;53:1258-1267.
28. Health Resources and Services Administration. Area Resource File. Available at: http://www.arfsys.com/overview.htm Accessed February 2009.
29. Hannan EL, Wu C, DeLong ER, Raudenbush SW. Predicting risk-adjusted mortality for CABG surgery: logistic versus hierarchical logistic models. *Med Care*. 2005;43:726-735.
30. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Available at: http://www. nccn.org/professionals/physician_gls/PDF/breast.pdf Accessed January 2009.
31. Gross CP, Smith BD, Wolf E, Andersen M. Racial disparities in cancer therapy: did the gap narrow between 1992 and 2002? *Cancer*. 2008;112:900-908.
32. Gelber RP, McCarthy EP, Davis JW, Seto TB. Ethnic disparities in breast cancer management among Asian Americans and Pacific Islanders. *Ann Surg Oncol*. 2006;13:977-984.
33. Freedman RA, Winer EP. Reducing disparities in breast cancer care: a daunting but essential responsibility. *J Natl Cancer Inst*. 2008;100:1661-1663.
34. Fontana V, Castro T, Polynice A. Preferences of healthy inner city women and the surgical treatment of early stage breast cancer. *Am Surg*. 2007;73:215-221.
35. Shih YC, Zhao L, Elting LS. Does Medicare coverage of colonoscopy reduce racial/ethnic disparities in cancer screening among the elderly? *Health Aff (Millwood)*. 2006; 25:1153-1162.
36. Bickell NA, LePar F, Wang JJ, Leventhal H. Lost opportunities: physicians' reasons and disparities in breast cancer treatment. *J Clin Oncol*. 2007;25:2516-2521.
37. Smith BD, Smith GL, Roberts KB, Buchholz TA. Baseline utilization of breast radiotherapy prior to institution of the Medicare Practice Quality Reporting Initiative. *Int J Radiat Oncol Biol Phys*. In press.
38. Smith GL, Smith BD, Haffty BG. Rationalization and regionalization of treatment for ductal carcinoma in situ of the breast. *Int J Radiat Oncol Biol Phys*. 2006;65:1397-1403.
39. Schroen AT, Brenin DR, Kelly MD, Knaus WA, Slingluff CL Jr. Impact of patient distance to radiation therapy on mastectomy use in early-stage breast cancer patients. *J Clin Oncol*. 2005;23:7074-7080.
40. Hershman DL, Buono D, McBride RB, et al. Surgeon characteristics and receipt of adjuvant radiotherapy in women with breast cancer. *J Natl Cancer Inst*. 2008;100: 199-206.
41. Jacobs LK, Kelley K, Chang D. Radiation therapy in urban and rural breast cancer patients [abstract]. Paper presented at 2008 ASCO Annual Meeting, May 30-June 3, 2008; Chicago, Illinois. Abstract 204A.
42. National Cancer Institute. NCI's Patient Navigator Research Program. Available at: http://www.cancer.gov/cancertopics/factsheet/PatientNavigator Accessed December 2008.
43. Halpern MT, Ward EM, Pavluck AL, Schrag NM, Bian J, Chen AY. Association of insurance status and ethnicity with cancer stage at diagnosis for 12 cancer sites: a retrospective analysis. *Lancet Oncol*. 2008;9:222-231.
44. Nattinger AB, Gottlieb MS, Veum J, Yahnke D, Goodwin JS. Geographic variation in the use of breast-conserving treatment for breast cancer. *N Engl J Med*. 1992;326:1102-1107.
45. Gilligan MA, Kneusel RT, Hoffmann RG, Greer AL, Nattinger AB. Persistent differences in sociodemographic determinants of breast conserving treatment despite overall increased adoption. *Med Care*. 2002;40:181-189.
46. Michalski TA, Nattinger AB. The influence of black race and socioeconomic status on the use of breast-conserving surgery for Medicare beneficiaries. *Cancer*. 1997;79(suppl): 314-319.

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METHODOLOGY Open Access

A method to predict breast cancer stage using Medicare claims

Grace L Smith[1], Ya-Chen T Shih[2], Sharon H Giordano[3], Benjamin D Smith[1,4], Thomas A Buchholz[1*]

Abstract

Background: In epidemiologic studies, cancer stage is an important predictor of outcomes. However, cancer stage is typically unavailable in medical insurance claims datasets, thus limiting the usefulness of such data for epidemiologic studies. Therefore, we sought to develop an algorithm to predict cancer stage based on covariates available from claims-based data.

Methods: We identified a cohort of 77,306 women age ≥ 66 years with stage I-IV breast cancer, using the Surveillence Epidemiology and End Results (SEER)-Medicare database. We formulated an algorithm to predict cancer stage using covariates (demographic, tumor, and treatment characteristics) obtained from claims. Logistic regression models derived prediction equations in a training set, and equations' test characteristics (sensitivity, specificity, positive predictive value (PPV), and negative predictive value [NPV]) were calculated in a validation set.

Results: Of the entire sample of women diagnosed with invasive breast cancer, 51% had stage I; 26% stage II; 11% stage III; and 4% stage IV disease. The equation predicting stage IV disease achieved sensitivity of 81%, specificity 89%, positive predictive value (PPV) 24%, and negative predictive value (NPV) 99%, while the equation distinguishing stage I/II from stage III disease achieved sensitivity 83%, specificity 78%, PPV 98%, and NPV 31%. Combined, the equations most accurately identified early stage disease and ascertained a sample in which 98% of patients were stage I or II.

Conclusions: A claims-based algorithm was utilized to predict breast cancer stage, and was particularly successful when used to identify early stage disease. These prediction equations may be applied in future studies of breast cancer patients, substantially improving the utility of claims-based studies in this group. This method may similarly be employed to develop algorithms permitting claims-based epidemiologic studies of patients with other cancers.

Background

Administrative medical insurance claims are an important source of population-based data used in epidemiologic studies of various diseases. Specifically, in older patients, national Medicare data have been useful for the study of many conditions, including myocardial infarction, heart failure, chronic kidney disease, Parkinson's disease, and venous thromboembolism [1-5]. However, for studying cancer, the use of national Medicare data has, to date, been limited. Medicare claims data are clearly recognized as potentially a rich source for cancer epidemiology and outcomes research, and in fact demonstrate acceptable validity for identifying cancer diagnoses and treatment patterns [6-13]. Unfortunately, the lack of cancer stage data in Medicare claims remains a major limiting factor in maximizing the utility of these datasets for retrospective, outcomes-based research in cancer patients[14,15]. In particular, cancer stage is a crucial predictor of disease outcome and a key factor in determining the appropriateness of treatment. For example, in breast cancer patients, stage is associated with overall and disease-free survival and, furthermore, stage influences treatment decisions such as selection and timing of surgery, radiotherapy, and chemotherapy [16]. Epidemiologic studies of cancer patients typically employ stage variables as covariates or as inclusion and exclusion criteria, and thus it is essential to develop accurate algorithms to account for cancer stage in studies using claims data.

Surprisingly, the need to derive such algorithms has largely been ignored in the literature. Only one prior

* Correspondence: tbuchhol@mdanderson.org
[1]Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd Houston, Texas 77030, USA

study has developed a claims-based algorithm to predict stage in breast cancer patients. Cooper et al. used the Surveillance Epidemiology and End Results (SEER)-Medicare database, and authors reported that their claims-based, single-predictor models were insufficient for identifying patients with local, regional, and distant stage disease. Sensitivity of these models for distinguishing local from regional and distant disease was low–for example, in breast cancer patient samples, only approximately 60%[17]. In the decade since the prior algorithm was derived, no other algorithm has been presented in the literature attempting to improve cancer stage classification using claims data. Thus studies have continued to apply the algorithm by Cooper and colleagues to derive cancer stage variables, despite the recognized limitations of this algorithm [18,19] and the introduction of measurement errors into such analyses.

Accordingly, we sought to derive an expanded predictive algorithm based on multivariate modeling and to improve the sensitivity and specificity for identifying cancer stage, using our study sample of breast cancer patients as an illustrative case. Using available Medicare claims for breast cancer patients found in the SEER-Medicare database, we developed a prediction algorithm to identify patients with distant (stage IV) disease at diagnosis and, among patients without distant disease, a prediction algorithm to classify the extent of locoregional (stages I-III) disease.

Methods

Algorithm

Study sample

The SEER-Medicare database is comprised of a population-based cohort of Medicare beneficiaries with incident cancer identified through SEER registries, which account for up to 26% of the United States' population [20,21]. Our initial study population consisted of 150,764 women (age ≥ 65 years) diagnosed with breast cancer between 1992 and 2002 identified through SEER-Medicare. From this population, we excluded 5,217 patients with unknown SEER historic stage (as this variable indicated the presence or absence of metastases), and 19,816 with *in situ* disease (as we intended to focus only on invasive disease). We further excluded 47,114 patients who did not have continuous Medicare Fee-for-Service coverage or had any HMO coverage from 12 months prior to 9 months after their diagnosis date (as claims information might be incomplete during these periods), and the 308 patients age <66, since these patients potentially would not have had comprehensive claims information to define the independent predictor covariates. We finally excluded 1,003 patients who died or were lost to follow-up within 9 months of their diagnosis date. This yielded a final sample size of 77,306 patients in our study.

Dependent variable: Cancer stage

The "gold standard" for identifying cancer stage at diagnosis was determined using a combination of tumor variables available through SEER. Distant disease was determined using the American Joint Committee on Cancer (AJCC) [22] historic stage as reported to SEER, which indicates tumor present in any distant site at cancer diagnosis (compared with tumor limited only to local or regional sites at diagnosis). For our analysis, patients with any distant disease were considered stage IV.

Patients without distant (stage IV) disease had local or regional AJCC historic stage. T and N classification in these patients were assigned based on SEER variables for tumor size and extent of disease. Tumor size and extent were categorized as ≤ 2 cm (T1); >2 to 5 cm (T2); >5 cm (T3); or invading into the chest wall, ribs, intercostals or serratus anterior muscles, extensive invasion into the skin, inflammatory carcinoma, or further contiguous extension into the skin (T4). Nodal disease was categorized as 0 positive lymph nodes (N0); 1-3 positive lymph nodes (N1); 4-9 positive lymph nodes (N2); or 10 or more positive lymph nodes (N3)[21]. Due to the extent of missing data in the SEER database, location of positive lymph nodes was not included in N classification. Stage I included T1N0 disease, stage II included T0N1, T1N1, T2N0, T2N1, and T3N0 disease, and stage III included T0-2N2, T3N1-2, T4N0-2, and T0-4N3 disease. These classifications are based on AJCC 2003 staging criteria[22].

Independent predictors

Candidate independent predictors were selected *a priori* based on statistical significance in bivariate analyses ($P < 0.25$) and clinical significance in prior studies of cancer patients[20,23-28]. Variables were defined by searching through inpatient, outpatient, and carrier Medicare claims or the denominator file for SEER-Medicare linked data for demographic variables. A comprehensive list of International Classification of Diseases, Ninth Revision (ICD-9), Common Procedural Terminology (CPT), and Revenue Center codes for each predictor are listed in Table S1, Additional file 1.

Statistical analysis

All statistical analyses were conducted using SAS version 9.1.3 (SAS Institute Inc, Cary, NC), and all statistical tests assumed a 2-tailed α of 0.05. The University of Texas M. D. Anderson Cancer Center institutional review board deemed this study exempt from review, since the data were without identifiers.

We derived two separate logistic models and implemented the models sequentially. The first model tested the associations between predictor covariates and the dichotomous outcome of stage IV versus non-stage IV disease. Among the subset of patients who were not categorized as having stage IV disease, the second

model tested the associations between predictor covariates (excluding the covariate for metastatic disease at diagnosis) and the dichotomous outcome of stage I/II (early) versus stage III disease. Outcomes were dichotomized based on clinical rationale, given that treatment of metastatic disease is palliative; and that treatment of early stage disease is distinct in that breast conserving therapy is a treatment option.

We used a split sample approach to develop and validate our logistic models. Each model was derived from the "training set," selected using simple random sampling without replacement (38,653 of 77,306 patients). Parsimonious models were then selected based on statistical significance ($P < 0.25$), clinical significance of covariates in prior studies,[20,23-28] and goodness-of-fit. Prior studies were used as an initial guide for the selection of covariates to consider. The significance cutoff ($P < 0.25$) was used to rule in covariates to keep. Examining the goodness-of-fit of the overall model was used to rule out covariates to exclude. In combination, these three criteria were used to select the final model.

Testing

Patients not included in the training set constituted the "validation set". In the validation set, the parameter associated with each covariate estimated from the derivation set was applied to each patient in the validation set to calculate each patient's predictive probability (calculated probability = $\exp(\hat{\beta}_0+\hat{\beta}_1 x_{1i}+\hat{\beta}_2 x_{2i}+\ldots) \Big/ 1+\exp(\hat{\beta}_0+\hat{\beta}_1 x_{2i}+\hat{\beta}_2 x_{2i}+\ldots)$) of having stage IV disease in the first model and stage I/II or stage III disease in the second model. Test characteristics were calculated for probability cutpoints between 0.05 and 0.90, using two-by-two tables. The "gold standard" for stage was considered the SEER stage; the test stage was based on the calculated probability (for example, for a probability cutpoint of 0.05, patients were predicted to have stage I/II disease if their calculated probability was ≥ 0.05, and not to have stage I/II disease if their calculated probability was <0.05).

Combining equations

The prediction equations were then applied to isolate a sample of patients with early stage disease. Specifically, the two prediction equations were applied sequentially to the validation sample in order to identify a subset of patients with stage I/II disease. The first step used a probability cutpoint of 0.05 to exclude patients with predicted stage IV disease. The second step was applied to the subset identified in the first step and used a probability cutpoint of 0.90 to include patients with predicted stage I/II disease. These cutpoints were chosen based on their test characteristics (high sensitivity, specificity, and positive predictive value [PPV] or negative predictive value [NPV]). Finally, we also compared the test characteristics derived from our multivariate prediction equations to test characteristics derived from single-predictor equations for distant and regional disease used in a prior study,[17] to determine whether multivariate equations improved test characteristics compared with the single-predictor equations.

Implementation

Example in Practice: Medicare test sample

Finally, we present an example that applies the prediction equation. We used a test sample based on a claims-only dataset, the national Medicare dataset. The national Medicare dataset includes claims data for all Medicare beneficiaries in the United States. Files contain data collected by Medicare for reimbursement of health care services for each beneficiary and include institutional (inpatient and outpatient) and non-institutional (physicians or other providers) final action claims [29]. We initially included 127,607 women (age ≥ 65) with a diagnosis claim indicating invasive breast cancer in 2003 (International Classification of Diseases, Ninth Revision (ICD-9) diagnosis code of 174) who underwent a breast-cancer related procedure. We then excluded 23,715 patients who did not have at least 2 claims (on different dates) specifying a diagnosis of invasive breast cancer between January 1, 2003 and December 31, 2004 (at least 1 claim must have occurred during 2003); 16,471 patients who had a breast cancer-related diagnosis or procedure claim between January 1, 2002, and December 31, 2002; 5,719 patients who were receiving Medicare coverage because of end-stage renal disease or disability; and 6,612 patients who lacked Part A or B coverage or who had intermittent health maintenance organization coverage in the 9 months after or in the 1 year before their breast cancer diagnosis date (of these patients, 3,561 had incomplete information in the year prior to diagnosis because they were <66 years of age); for a total sample size of 56,725 patients. This method for sample selection of incident breast cancer has been validated in a prior study [30].

In this test sample, we applied our derived algorithm and calculated the frequency of patients classified as predicted stage IV and predicted stage I/II disease. Again, for this sample, the first step used a probability cutpoint of 0.05 and the second step a probability cutpoint of 0.90. As a test of our algorithm for consistency, we compared the predicted frequencies to the actual stage distribution in two populations: 1) the SEER-Medicare population (age >65 years) and 2) the National Cancer Data Base population (age ≥ 70 years) [31].

Results

Patient characteristics

In 77,306 women, mean age was 76 years (standard deviation 7 years), and 94% were white. Fifty-one percent were stage I (39,147), 26% stage II (19,967), 11% stage III (8,174), 4% stage IV (3,220) and 9% with non-

distant disease but T or N classification unknown (6,798). Forty-five percent were treated with breast conserving surgery, 49% with mastectomy, 44% with radiotherapy, and 18% with chemotherapy (Table 1).

Prediction algorithm equations and test characteristics for probability cutpoints

Candidate covariates tested in prediction equations are listed in Table S1, Additional file 1. Parameter estimates for the covariates included in each final prediction equation are listed in Table S2, Additional file 1.

Stage IV

Fourteen percent of all patients and 73% of patients with stage IV disease had a claims code indicating possible metastatic disease. Accordingly, the single-predictor model including only this covariate had sensitivity of 73%; specificity 89%; PPV 22%; and NPV 99% for identifying stage IV disease. After including covariates (Table S2, Additional file 1) in the multivariate model, the sensitivity was 81% (95% Confidence Interval 80% - 84%) for identifying stage IV disease at a probability cutpoint of 0.05. At this cutpoint, specificity was 89% (86% - 89%); PPV 24%; (22% - 25%) and NPV 99% (99% - 99%), yielding a c-statistic of 0.93. (Table S3, Additional file 1) The distribution of calculated predicted probabilities in the validation set for patients with stage IV versus stage I-III disease is presented in Figure 1a.

Table 1 Study Sample Patient Characteristics, N = 77,306

Predictor Variable	% of All Patients
Demographic	
Age, mean (SD)	76 (7)
White race	94
Stage	
Stage I	51
Stage II	26
Stage III	10
Stage IV	4
Stages I-III but T or N unknown	9
Extent of disease[a]	
Axillary LN involvement	19
Metastatic disease	14
Cancer treatment[a]	
No. visits to surgeon, mean (SD)	4 (3)
No. visits to medical oncologist, mean (SD)	4 (9)
No. visits to radiation oncologist, mean (SD)	3 (5)
Imaging (CT, MRI, PET, or bone scan)	25
Radiation therapy	44
Breast conserving surgery	45
Mastectomy	49
Axillary LN dissection	72
Chemotherapy (any agent)	18
Doxorubicin	7
Paclitaxel	3
No. physician visits, mean (SD)	14 (12)
Screening mammography	78
Influenza vaccine	34
General health status[a]	
No. hospital admission for any cause, mean (SD)	1 (1)
Charlson comorbidity score	
0 comorbid conditions	69
1 comorbid condition	18
2 or more comorbid conditions	8
Unknown	5

Abbreviations: CT computed tomography; LN lymph nodes; MRI magnetic resonance imaging PET positron emission tomography; SD standard deviation
[a] As indicated by Medicare claims codes; thus percentage of patients with code for metastatic disease not equal to patients with Stage IV disease.

Stages I-III

In patients with stages I-III disease, 19% had a claims code indicating axillary lymph node involvement. Specifically, 2% of patients with stage I disease, 36% with stage II disease, and 64% of patients with stage III disease had this claims code. The single-predictor model including only this covariate yielded sensitivity of 87% (specificity 61%; PPV 94%; NPV 39%) for identifying stage I/II disease and sensitivity of 61% (and specificity 87%; PPV 39%; NPV 94%) for identifying stage III disease. After including covariates (Table S2, Additional file 1) in the multivariate model, the sensitivity was 91% (90% - 92%) for identifying stage I/II disease at a probability cutpoint of 0.80; and 83% (83% - 85%) at a cutpoint of 0.90. At a cutpoint of 0.90, specificity was 78% (75% - 79%); PPV 98% (97% - 98%); and NPV 31% (30% - 34%). For identifying stage III disease, the sensitivity was 78% (75% - 79%) at a cutpoint of 0.10. At this cutpoint, specificity was 83% (83% - 85%); PPV 30% (30% - 34%); and NPV 98% (97% - 98%) (Table S3, Additional file 1). These models yielded a c-statistic of 0.88. The distribution of calculated predicted probabilities in the validation set for patients with stage I/II versus stage III disease is presented in Figure 1b.

Comparison with other single predictors

For comparison's sake, for identifying stage IV disease, the second most important predictor was axillary lymph node dissection. This predictor alone would yield the following test characteristics: sensitivity 67%; specificity 74%; PPV 10%; and NPV 98%. For identifying stage I/II disease, the second most important predictor was breast conserving surgery vs. mastectomy, yielding the following test characteristics: sensitivity 49%; specificity 82%; PPV 95%; and NPV 18%.

Combining equations

The prediction equations were most accurate for isolating patients with early stage disease. Specifically, after applying the two prediction equations sequentially to the validation sample to identify patients with predicted stage I/II disease, a subset of 23,285 patients were selected (of 38,653 patients, 36,417 were predicted to

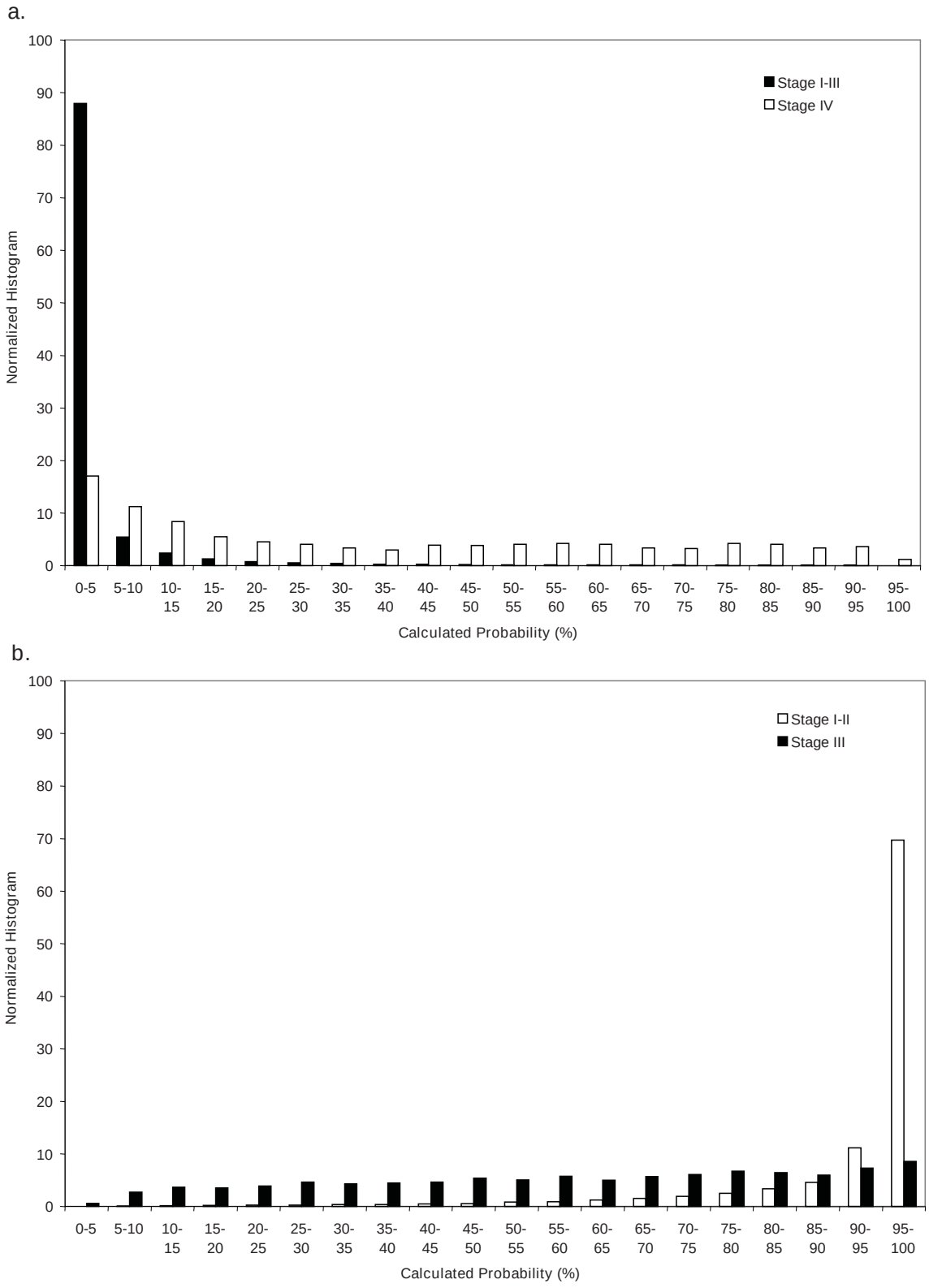

Figure 1 Distribution of calculated probabilities (%) for patients with predicted stages I-III and stage IV disease (a). Distribution of calculated probabilities for patients with predicted stages I-II and stage III disease (b). A calculated probability of 5% corresponds to a cutpoint of 0.05. The histograms are normalized to 100%.

have non-stage IV disease, and of these patients, 23,285 were predicted to have stage I/II disease). The predictive sample actually consisted of 98% gold standard stage I/II disease (22,706 of 23,285), 2% stage III disease (549 of 23,285), and <1% stage IV disease (110 of 23,285). Of all patients with gold standard stage I/II disease (29,546 of 38,653 validation patients), 23% (6,840 of 29,546) were excluded (classified as other than stage I/II) as a result of the algorithm (4,604 from the first model and 2,236 from the second model). (Figure 2, Figure 3).

Example in Practice: Medicare test sample and comparison for consistency

In our Medicare test sample, after the first predictor equation was applied, a total of 4% (2,333 of 56,725) of women were predicted as having stage IV disease. This compared favorably with the SEER-Medicare population, which included 4% (3,220 of 77,306) of women with confirmed stage IV disease; as well as the NCDB population, which included 5% (1,913 of 41,071) confirmed stage IV disease. After the second predictor equation was applied to the remainder of the test sample, a total of 79% (43,169 of 54,392) of women were predicted as having stage I/II disease. This compared favorably with the SEER-Medicare population, which included 80% (59,114 of 74,086) of women with confirmed Stage I/II disease; as well as the NCDB population, which included 84% (33,036 of 39,158) confirmed Stage I/II disease.

Discussion

In this cohort of older breast cancer patients, Medicare claims data assisted the prediction of cancer stage. Predictor equations using claims data alone were able to achieve approximately 80% sensitivity and specificity for identifying stage IV disease as well as distinguishing stage I/II from stage III disease. Prediction models maximized NPV when distinguishing stage IV from stage I-III disease but maximized PPV when distinguishing stage I/II from III disease. With a resulting tradeoff of lower PPV in the first model and lower NPV in the second model, the algorithm was therefore found to be best suited to most accurately identify early stage disease. Specifically, an algorithm combining the two equations seeking to identify patients with early stage disease was able to achieve a sample in which 98% of patients had stage I or II disease.

Our prediction models represent an improvement over the single other previously published model. In this prior study, Cooper et al. used single-predictor equations to identify cancer stage. To identify patients with distant disease, authors tested a single variable based on claims codes for metastatic disease. This single-predictor model demonstrated 60% sensitivity and 58% PPV. To distinguish patients with local versus regional disease, authors tested a single variable based on the claim code for axillary lymph node involvement. This single-predictor model demonstrated 62% sensitivity and 85% PPV [17]. The relatively poor test characteristics from this prior study demonstrated that these single-predictor models would be insufficient for predicting stage in patients with breast cancer and suggested that claims data alone would be inadequate for epidemiologic studies of cancer patients.

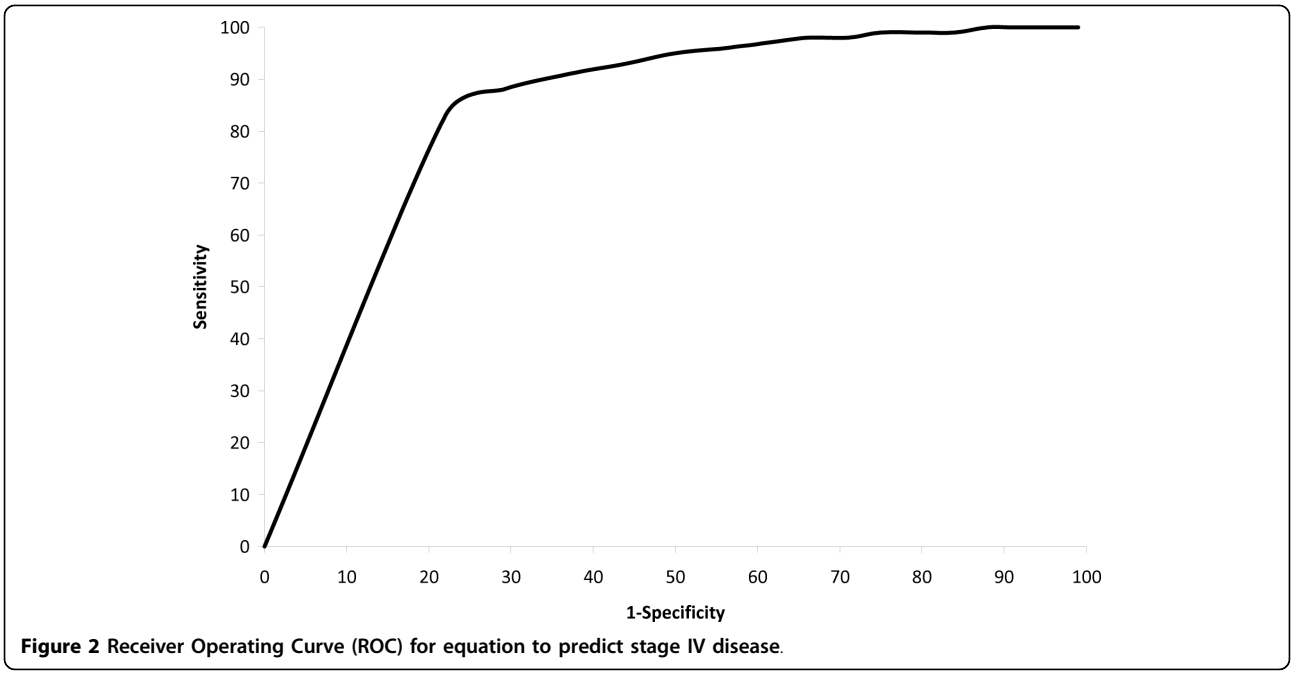

Figure 2 Receiver Operating Curve (ROC) for equation to predict stage IV disease.

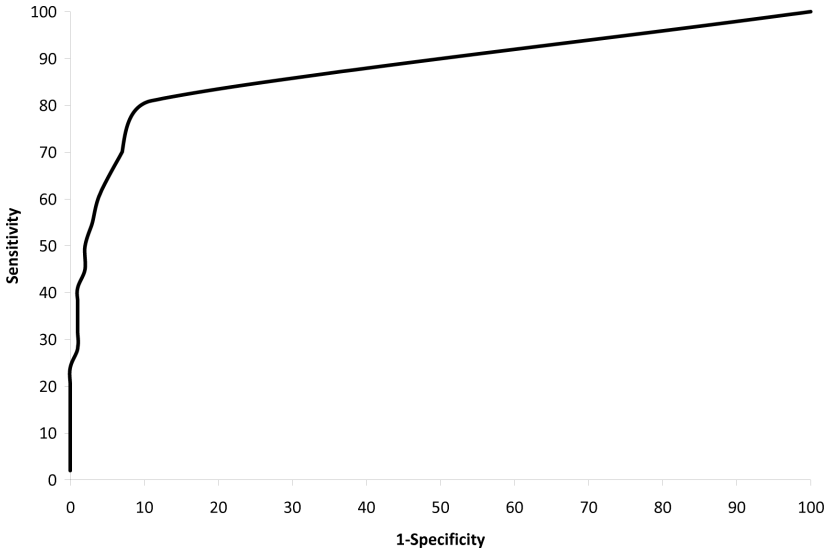

Figure 3 Receiver Operating Curve (ROC) for equation to predict stage I-III disease.

In contrast, our prediction models have improved upon these test characteristics. Our single predictor model demonstrated improvement, likely in part due to a more extensive list of claims codes, with multiple covariates providing added value. Moreover, our algorithm demonstrated consistency when results were compared with population-based data from SEER-Medicare and the NCDB. There are two important future research applications of our prediction models. First, our multivariate logistic modeling method for developing a stage predictor algorithm may similarly be applied to test models and potentially develop stage prediction equations for patients diagnosed with cancers of other sites. Second, our prediction equations may also be applied directly to claims-based databases of breast cancer patients who have unknown stage. Using a combination of multiple predictors along with claims codes for metastatic disease and axillary lymph node dissection, parameter estimates and calculated probabilities can be applied to the prediction of patient breast cancer stage.

Our algorithm can therefore serve as a tool to assist in the investigation of a variety of epidemiologic research questions in breast cancer patients by allowing a sample selection of those patients with early stage disease. In addition, predicted early stage disease can be applied as a covariate. Accordingly, since disease stage may be better accounted for, claims databases of breast cancer patients may also be better applied to address such questions as the assessment of treatment utilization, geographic variation, or outcomes in patients diagnosed with early stage breast cancer. Specifically, for the stage IV prediction model, a probability cutpoint between ≥ 0.05 and ≥ 0.10 would be highly specific and sensitive for identifying patients with stage IV disease. For the stage I/II prediction model, a cutpoint between ≥ 0.80 and ≥ 0.90 would be highly specific and sensitive for distinguishing patients with stage I/II disease from patients with stage III disease.

For the identification of patients with stage IV disease, a selected probability cutpoint criterion could be translated into a dichotomous variable, and used either to select a sample of patients with stage IV disease or used in a "rule out" context, as an exclusion criterion. The high NPV in our proposed model suggests that when using these cutpoints to identify a sample limited to patients with stage I-III disease, the likelihood of misclassification bias (bias due to the inappropriate inclusion of patients with stage IV disease in the sample) would be low in a "rule-out" setting.

For distinguishing patients with stage I/II versus III disease, the probability cutpoint criterion, translated into a dichotomous variable, could be useful in various contexts, such as excluding patients with stage III disease in order to refine a study population of patients with early stage breast cancer, or creating a dichotomous covariate to adjust for potential confounding associated with stage I-III disease. The test characteristics in our analysis suggest that the combination of these prediction equations may be particularly useful in the context of identifying breast cancer patients with early stage (stage I and II) disease.

Our study has limitations to consider. First, our cohort was limited only to older patients with breast cancer. Although the variables associated with stage are likely to be similar in younger patients, exact parameter estimates may differ, and the application of these models in younger patients requires further validation. Additionally,

as our predictor variables were derived from Medicare claims, these models will also require validation in other claims based data. If not all the proposed variables in our models are available, however, at a minimum, adjustment in multivariate analysis for as many possible available candidate predictors proposed in our study could be useful to improve modeling of breast cancer outcomes in future studies. Although we excluded from our parsimonious model covariates that required long-term follow-up (specifically, overall survival and mastectomy 9 or more months after diagnosis), our models still required both retrospective and prospective data for up to 1 year prior to and 1 year after the date of diagnosis. Thus, studies applying our models would be limited to patients with continuous coverage and complete claims information over this time period. The gold standard for our outcome, cancer stage, was based on pathologic variables in SEER-Medicare, though given a lack of central pathology review by the SEER program, unmeasured error may have affected the gold standard, yielding potentially less than 100% accuracy. Finally, if a sample was selected based on the algorithm, sample characteristics derived from algorithm predictor variables (for example, chemotherapy, radiotherapy, and surgery utilization) may be under- or overestimated compared with the complete patient population, depending on the direction and significance of their association with disease stage in the prediction equations.

Conclusions

Medicare claims data can be utilized to derive a useful algorithm to predict stage in breast cancer patients. In particular, the predicted probability of early stage disease can be easily generated when applying the prediction algorithm to this patient population, thus substantially improving the utility of Medicare claims data for studying breast cancer.

Additional file 1: Table S1. Candidate Covariates and Claims Codes. Table S2. Prediction Equations. Parameter estimates for stage IV versus stages I-III disease and for stage. I/II versus stage III disease. Table S3. Test Characteristics After Applying Prediction Equations on Validation Set Samples.
Click here for file
[http://www.biomedcentral.com/content/supplementary/1742-5573-7-1-S1.DOC]

Abbreviations

AJCC: American Joint Committee on Cancer; SEER: Surveillance Epidemiology and End Results; PPV: Positive predictive value; NPV: Negative predictive value; ICD-9: International Classification of Diseases, Ninth Revision; CPT: Current Procedural Terminology.

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Author details

[1]Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd Houston, Texas 77030, USA. [2]Department of Biostatistics, Section of Health Services Research, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, Texas 77030, USA. [3]Department of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, Texas 77030, USA. [4]Radiation Oncology Flight, Wilford Hall Medical Center, Lackland Air Force Base, San Antonio, Texas 78236, USA.

Authors' contributions

GLS helped to design the study, conduct the statistical analysis and interpret the results, and drafted the manuscript. YCTS helped to design the study and analysis, gave substantial input on the statistical design, helped to interpret the results, and gave critical revisions for manuscript content. SHG contributed to study conception, interpret the statistical analysis and results, and gave critical revisions for manuscript content. BDS helped to design the study, acquire the data, interpret the statistical analysis and results, and gave critical revisions for manuscript content. TAB contributed to study conception and design, interpret the statistical analysis and results, and gave critical revisions for manuscript content. All authors have given final approval of this manuscript.

Competing interests

The authors declare that they have no competing interests.

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References

1. Goff DC Jr, Pandey DK, Chan FA, Ortiz C, Nichaman MZ: **Congestive heart failure in the United States: is there more than meets the I(CD code)? The Corpus Christi Heart Project.** *Arch Intern Med* 2000, **160**:197-202.
2. Kiyota Y, Schneeweiss S, Glynn RJ, Cannuscio CC, Avorn J, Solomon DH: **Accuracy of Medicare claims-based diagnosis of acute myocardial infarction: estimating positive predictive value on the basis of review of hospital records.** *Am Heart J* 2004, **148**:99-104.
3. Leibson CL, Needleman J, Buerhaus P, Heit JA, Melton LJ, Naessens JM, Bailey KR, Petterson TM, Ransom JE, Harris MR: **Identifying in-hospital venous thromboembolism (VTE): a comparison of claims-based approaches with the Rochester Epidemiology Project VTE cohort.** *Med Care* 2008, **46**:127-132.
4. Noyes K, Liu H, Holloway R, Dick AW: **Accuracy of Medicare claims data in identifying Parkinsonism cases: comparison with the Medicare current beneficiary survey.** *Mov Disord* 2007, **22**:509-514.
5. Winkelmayer WC, Schneeweiss S, Mogun H, Patrick AR, Avorn J, Solomon DH: **Identification of individuals with CKD from Medicare claims data: a validation study.** *Am J Kidney Dis* 2005, **46**:225-232.
6. Cooper GS, Virnig B, Klabunde CN, Schussler N, Freeman J, Warren JL: **Use of SEER-Medicare data for measuring cancer surgery.** *Med Care* 2002, **40**:43-48.
7. Cooper GS, Yuan Z, Stange KC, Dennis LK, Amini SB, Rimm AA: **Agreement of Medicare claims and tumor registry data for assessment of cancer-related treatment.** *Med Care* 2000, **38**:411-421.
8. Du X, Freeman JL, Goodwin JS: **Information on radiation treatment in patients with breast cancer: the advantages of the linked medicare and**

SEER data. Surveillance, Epidemiology and End Results. *J Clin Epidemiol* 1999, **52**:463-470.
9. Du X, Goodwin JS: **Patterns of use of chemotherapy for breast cancer in older women: findings from Medicare claims data.** *J Clin Oncol* 2001, **19**:1455-1461.
10. Du XL, Chan W, Giordano S, Geraci JM, Delclos GL, Burau K, Fang S: **Variation in modes of chemotherapy administration for breast carcinoma and association with hospitalization for chemotherapy-related toxicity.** *Cancer* 2005, **104**:913-924.
11. Nattinger AB, Laud PW, Bajorunaite R, Sparapani RA, Freeman JL: **An algorithm for the use of Medicare claims data to identify women with incident breast cancer.** *Health Serv Res* 2004, **39**:1733-1749.
12. Virnig BA, Warren JL, Cooper GS, Klabunde CN, Schussler N, Freeman J: **Studying radiation therapy using SEER-Medicare-linked data.** *Med Care* 2002, **40**:49-54.
13. Warren JL, Harlan LC, Fahey A, Virnig BA, Freeman JL, Klabunde CN, Cooper GS, Knopf KB: **Utility of the SEER-Medicare data to identify chemotherapy use.** *Med Care* 2002, **40**:55-61.
14. Ko CY, Parikh J, Zingmond D: **Secondary analyses of large population-based data sets: issues of quality, standards, and understanding.** *Ann Surg Oncol* 2008, **15**:395-396.
15. Nathan H, Pawlik TM: **Limitations of claims and registry data in surgical oncology research.** *Ann Surg Oncol* 2008, **15**:415-423.
16. Woodward WA, Strom EA, Tucker SL, McNeese MD, Perkins GH, Schechter NR, Singletary SE, Theriault RL, Hortobagyi GN, Hunt KK, Buchholz TA: **Changes in the 2003 American Joint Committee on Cancer staging for breast cancer dramatically affect stage-specific survival.** *J Clin Oncol* 2003, **21**:3244-3248.
17. Cooper GS, Yuan Z, Stange KC, Amini SB, Dennis LK, Rimm AA: **The utility of Medicare claims data for measuring cancer stage.** *Med Care* 1999, **37**:706-711.
18. Gozalo PL, Miller SC: **Hospice enrollment and evaluation of its causal effect on hospitalization of dying nursing home patients.** *Health Serv Res* 2007, **42**:587-610.
19. Case C, Johantgen M, Steiner C: **Outpatient mastectomy: clinical, payer, and geographic influences.** *Health Serv Res* 2001, **36**:869-884.
20. Smith BD, Gross CP, Smith GL, Galusha DH, Bekelman JE, Haffty BG: **Effectiveness of radiation therapy for older women with early breast cancer.** *J Natl Cancer Inst* 2006, **98**:681-690.
21. **US Department of Health and Human Services Cancer Statistics Branch. SEER Manuals Extent of Disease–1998 Codes and Coding Instructions [National Cancer Institute Surveillance Epidemiology and End Results web site].** 1998http://www.seer.cancer.gov/manuals/EOD10Dig.3rd.pdf.
22. Greene FL, Page DL, Fleming ID: *AJCC Cancer Staging Manual* New York: Springer Science & Business Media, 6 2003.
23. Smith BD, Haffty BG, Buchholz TA, Smith GL, Galusha DH, Bekelman JE, Gross CP: **Effectiveness of radiation therapy in older women with ductal carcinoma in situ.** *J Natl Cancer Inst* 2006, **98**:1302-1310.
24. Smith BD, Haffty BG, Smith GL, Hurria A, Buchholz TA, Gross CP: **Use of postmastectomy radiotherapy in older women.** *Int J Radiat Oncol Biol Phys* 2008, **71**:98-106.
25. Smith BD, Smith GL, Buchholz TA: **Controversies over the role of radiation therapy for ductal carcinoma in situ.** *Expert Rev Anticancer Ther* 2008, **8**:433-441.
26. Smith BD, Smith GL, Haffty BG: **Postmastectomy radiation and mortality in women with T1-2 node-positive breast cancer.** *J Clin Oncol* 2005, **23**:1409-1419.
27. Smith GL, Smith BD, Giordano SH, Shih YC, Woodward WA, Strom EA, Perkins GH, Tereffe W, Yu TK, Buchholz TA: **Risk of hypothyroidism in older breast cancer patients treated with radiation.** *Cancer* 2008, **112**:1371-1379.
28. Klabunde CN, Potosky AL, Legler JM, Warren JL: **Development of a comorbidity index using physician claims data.** *J Clin Epidemiol* 2000, **53**:1258-1267.
29. **Research Data Assistance Center: Medicare data available.** http://www.resdac.umn.edu/Medicare/data_available.asp, Accessed April 2009.
30. Nattinger AB, Laud PW, Bajorunaite R, Sparapani RA, Freeman JL: **An algorithm for the use of Medicare claims data to identify women with incident breast cancer.** *Health Serv Res* 2004, **39**:1733-49.
31. **National Cancer Data Base (NCDB).** http://cromwell.facs.org/BMarks/BMPub/Ver10/DxRx/BMPub_DxRx.cfm, Accessed April 2009.

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Breast-Conserving Surgery in Older Patients with Invasive Breast Cancer: Current Patterns of Treatment Across the United States

Grace L Smith, MD, PhD, Ying Xu, MD, MS, Ya-Chen T Shih, PhD, Sharon H Giordano, MD, MPH, Benjamin D Smith, MD, Kelly K Hunt, MD, FACS, Eric A Strom, MD, George H Perkins, MD, Gabriel N Hortobagyi, MD, Thomas A Buchholz, MD

BACKGROUND: Breast-conserving surgery (BCS) followed by radiotherapy is as effective as mastectomy for treatment of early invasive breast cancer. But earlier studies report low BCS use rates of 12% to 43% nationally, especially in older patients. We sought to determine current patterns and predictors of BCS use.

STUDY DESIGN: In a national Medicare database of all beneficiaries (age greater than 65 years) with incident invasive breast cancer treated with operation in 2003, claims codes identified BCS versus mastectomy and demographic, treatment, and geographic region covariates. The 2003 Area Resource File provided socioeconomic covariates. Logistic regression modeled predictors of BCS.

RESULTS: In 56,725 women, 59% were treated with BCS versus 41% with mastectomy. BCS was more likely in women who were younger than 70 years (odds ratio [OR], 1.37; 95% CI, 1.31 to 1.44; $p < 0.001$) and had lymph node-negative disease (OR, 1.60; 95% CI, 1.52 to 1.68; $p < 0.001$). Socioeconomic factors influenced use, with BCS more likely in areas with low poverty (OR, 1.05; 95% CI, 1.00 to 1.09; $p = 0.03$), high education (OR, 1.13; 95% CI, 1.08 to 1.19), high density of radiation oncologists (OR, 1.30; 95% CI, 1.06 to 1.59), and in metropolitan areas (OR, 1.20; 95% CI, 1.14 to 1.26). Significant geographic variation existed: 70% of women were treated with BCS in northeastern New England compared with only 48% to 50% in the South ($p < 0.001$).

CONCLUSIONS: Currently, more than half of older women across the US diagnosed with nonmetastatic invasive breast cancer treated surgically receive BCS, representing a substantial increased use compared with historical data. Lack of BCS use appears in part associated with socioeconomic disadvantage, suggesting that persistent barriers to breast conservation exist. (J Am Coll Surg 2009;209: 425–433. © 2009 by the American College of Surgeons)

In patients diagnosed with invasive breast cancer, breast-conserving surgery (BCS) followed by radiotherapy (RT) is considered as effective as mastectomy for treatment of early-stage disease.[1] Cumulative data from randomized trials demonstrate that patients treated with breast-conserving therapy have overall survival rates comparable to those in patients treated with mastectomy.[2,3] A 20-year update of the National Surgical Adjuvant Breast and Bowel Project (NSABP)-B06 trial affirmed that these treatment options were still comparable even on longterm followup.[2] Given the strong evidence supporting the effectiveness of breast-conserving therapy for treating early-stage disease, many experts have recommended that this option be selected, when possible, in order to promote breast conservation.[3-5]

Despite the recommendations supporting breast-conserving therapy, studies of breast cancer patients treated in the 1980s and 1990s reported low rates of BCS, with less than half of all surgically treated patients with nonmetastatic invasive disease receiving BCS.[6,7] These studies noted sig-

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From the Department of Radiation Oncology (GL Smith, BD Smith, Strom, Perkins, Buchholz), the Section of Health Services Research, Department of Biostatistics (Xu, Shih), and the Departments of Breast Medical Oncology (Giordano, Hortobagyi) and Surgical Oncology (Hunt), the University of Texas MD Anderson Cancer Center, Houston, TX; and the Radiation Oncology Flight (BD Smith), Wilford Hall Medical Center, Lackland AFB, TX. Correspondence address: Thomas A Buchholz, MD, Department of Radiation Oncology, University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Unit 97, Houston, TX 77030.

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Abbreviations and Acronyms

BCS = breast-conserving surgery
NSABP = National Surgical Adjuvant Breast and Bowel Project
OR = odds ratio
RT = radiotherapy
SEER = Surveillance, Epidemiology, and End Results

nificant geographic variation in treatment, but even in regions with the highest use, only about 40% of patients were treated with BCS.[6] Results further suggested that during these earlier eras, significant treatment disparities existed, with non-Caucasian patients and patients facing healthcare access barriers less likely to receive BCS.[5-9]

Contemporary data are lacking. It is unclear whether more recently the frequency of BCS has surpassed mastectomy use and whether rates of BCS have increased in regions of the US previously demonstrating low rates. In addition, it is not known whether socioeconomic factors continue to be strong influential factors affecting treatment. Characterizing contemporary use patterns is important for identifying persistent barriers to treatment with BCS. So, in a contemporary national sample of Medicare patients diagnosed with invasive breast cancer, we sought to quantify the frequency of treatment with BCS versus mastectomy. In addition, we sought to determine whether socioeconomic and demographic factors—such as geographic region, income, education, and the supply of health-care providers—influenced surgical treatment in patients across the US.

METHODS

National Medicare dataset and study sample derivation

The national Medicare dataset includes claims data for all Medicare beneficiaries in the US. Files contain data collected by Medicare for reimbursement of health-care services for each beneficiary and include institutional (inpatient and outpatient) and noninstitutional (physicians or other providers) final action claims.[7] Of note, the national Medicare dataset is distinct from the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database;[10] our Medicare dataset is nationally comprehensive and SEER-Medicare focuses only on select SEER registry sites. The University of Texas MD Anderson Cancer Center's institutional review board exempted use of the Medicare database for this study.

We used the following algorithm to identify patients with incident breast cancer, treated with either BCS or mastectomy. This method was based on a previous validated algorithm for claims data.[11,12] We included women (age 65 years or more) who had any diagnosis of invasive breast cancer in 2003 (defined as an ICD-9 diagnosis code of 174) who underwent BCS (n = 83,611) or mastectomy (n = 42,504) between January 1, 2003, and December 31, 2003. From this sample, to increase the specificity of the definition, we excluded 23,715 patients who did not have at least 2 claims (on different dates) indicating a diagnosis of invasive breast cancer between January 1, 2003, and December 31, 2004 (at least 1 claim must have occurred during 2003), with no more than 6 months between the date of BCS or mastectomy and the earliest breast cancer diagnosis claim date. To exclude the prevalent cases, we excluded 16,471 patients who had a breast cancer-related diagnosis or procedure claim between January 1, 2002, and December 31, 2002. To reduce misclassification of the primary intended operation, we excluded 630 patients who underwent both types of operation (either date of mastectomy claim preceding date of BCS claim or mastectomy occurring more than 3 months after BCS), except for patients who received a mastectomy within 3 months of BCS and for whom mastectomy was considered the definitive operation. To limit our sample to patients with nonmetastatic invasive breast cancer, we then excluded 2,122 patients who had 2 or more claims specifying metastatic breast cancer from 3 months before to 3 months after the diagnosis date. To improve sample homogeneity, we also excluded 5,719 patients who were receiving Medicare coverage because of end-stage renal disease or disability. Finally, to ensure we had complete claims information to determine patients' cancer treatment course and comorbidities, we excluded 6,612 patients who lacked part A or B coverage or who had intermittent health maintenance organization coverage in the 9 months after or in the 1 year before their breast cancer diagnosis date (of these patients, 3,561 had incomplete information in the year before diagnosis, because they were less than 66 years of age). For this analysis, the breast cancer diagnosis date was defined as the date of the earliest claim for a diagnosis of breast cancer. This left a final sample size of 56,725 patients.

Surgical treatment and other covariates

Covariates derived from Medicare files (denominator and claims files) included cancer treatment variables, other clinical variables, and demographic data. Patients were classified as treated with BCS or mastectomy if a claim for the operation (Appendix, online) occurred within 6 months of the breast cancer diagnosis date. Claims for chemotherapy must have occurred within 6 months and RT claims within

9 months of the breast cancer diagnosis date. These claims-based treatment definitions have been applied in previous studies of breast cancer patients.[13-18]

Other disease- and treatment-related variables included axillary lymph node involvement, axillary lymph node dissection, sentinel node biopsy, receipt of any chemotherapy, specific receipt of doxorubicin or paclitaxel, receipt of any imaging studies for staging, number of hospitalizations in the year after diagnosis, and number of medical oncology, radiation oncology, and surgery visits in the year after diagnosis. Variables indicating preventive health care and interactions with the health-care system included mammography in the year before diagnosis and number of physician visits in the year before diagnosis. In addition, we calculated the severity of comorbid disease for each patient based on a modified Charlson comorbidity score validated in an earlier claims-based study: 0 (no comorbidity), 1 (mild to moderate), or 2 or more (severe).[19] This score combined comorbidities recorded in Medicare claims during the 12 months before the patient's cancer diagnosis. To enhance specificity of comorbid disease diagnoses, patients must have had at least 1 inpatient (part A) claim or at least 2 outpatient (part B) claims more than 30 days apart.[19]

Demographic data available through Medicare files included patient age at diagnosis, race (categorized as Caucasian, African American, and other), and state and county of residence. Classification of geographic regions was based on US Census Division definitions.[20] Socioeconomic variables, obtained from the 2003 Area Resource File[21] and linked to the Medicare dataset by county of patient's residence, included median household income, percent living below poverty level, and percent completing ninth grade education, high school, or college. Supply of health-care providers (for breast cancer treatment) was measured by the density of general surgeons and of radiation oncologists at county level, obtained from the 2003 Area Resource File.

Statistical analysis

All analyses were conducted using SAS software version 9.1.3 (SAS Institute), and all statistical tests assumed a 2-tailed α of 0.05. We calculated percent BCS versus mastectomy use for the entire sample, by state and by region. We also tested the unadjusted bivariate associations between receipt of BCS and treatment, clinical, demographic, and socioeconomic covariates using the Pearson chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables.

A multivariate logistic model tested adjusted associations between BCS and covariates. Covariates for the final multivariate model were initially selected a priori based on significance in bivariate analyses ($p < 0.25$) and significance in earlier studies of cancer patients.[19-24] The final parsimonious model was selected based on statistical significance, goodness of fit, and minimizing multicollinearity. This model was also used to calculate adjusted rates of BCS use by state. Goodness of fit was assessed based on the model R-square value and the Hosmer-Lemeshow test.

Early-stage breast cancer subgroup

Breast cancer stage is not directly available through Medicare claims data. To select a subgroup of patients with early-stage breast cancer, given that surgical treatment strategies are typically dependent on disease stage, we applied a previously validated predictive algorithm that used claims-based covariates to identify patients with a high probability of having stage I or II disease (unpublished data; Appendix, online). So, in the selected subgroup of 43,706 predicted early-stage patients, we further examined the adjusted associations between receipt of BCS and covariates using multivariate logistic modeling.

In a secondary, validating analysis on this selected group of predicted early-stage patients, we also identified the subgroup of 42,499 patients who did not have claims for axillary involvement and chemotherapy; these patients would also be more likely to have early-stage disease (kappa = 0.73 for the 2 selected subgroups). The adjusted associations were compared in this group with the associations calculated for the predicted early-stage patients.

RESULTS

Patient characteristics and treatment course

Our cohort consisted of 56,725 women with incident, invasive breast cancer diagnosed in 2003 and treated with surgery. In our sample, median age was 76 years (interquartile range, 71 to 81 years). Ninety percent (n = 51,432) were Caucasian, 7% (n = 3,727) were African American, and 3% (n = 1,566) were of other race. As a component of the initial treatment course, the majority of patients were treated with BCS. Specifically, 59% of patients (n = 33,450) received BCS, and 41% (n = 23,275) underwent mastectomy. Additionally, of the entire sample, 50% received RT and 16% received chemotherapy. Of BCS patients, 74% received RT and 13% received chemotherapy. Of mastectomy patients, 14% received RT and 23% chemotherapy.

Predictors of breast-conserving surgery versus mastectomy use

The use of BCS was associated with both clinical and nonclinical factors. In the entire sample, on unadjusted analysis, patients who were younger, Caucasian, had fewer comorbidities, lymph node-negative disease, and predicted

Table 1. Patient Characteristics and Use of Breast-Conserving Surgery Versus Mastectomy in Women (n = 56,725)

	Treated with BCS		Treated with mastectomy	
Patient characteristic	**n**	**%**	**n**	**%**
Demographic				
Age, y, mean (SD)	76 (7)		77 (7)	
66 to < 70	63	7,112	37	4,260
≥ 70	58	26,338	42	19,015
Race				
Caucasian	59	30,572	41	20,860
African American	54	2,026	46	1,701
Other	54	852	46	714
Clinical				
Charlson comorbidity score				
0 comorbid conditions	61	22,735	39	14,578
1 comorbid condition	57	6,414	43	4,875
2 or more comorbid conditions	54	2,673	46	2,314
Unknown	52	1,628	48	1,508
Disease stage and treatment				
Predicted early-stage (stage I or II) disease	68	29,828	32	3,622
Axillary lymph node-positive disease	37	17,587	63	30,050
Lymph node-negative disease	63	5,688	37	3,400
Axillary lymph node dissection	42	11,995	58	16,715
No axillary dissection	77	21,455	23	6,560
Radiation therapy	88	24,823	12	3,358
No radiation therapy	30	8,627	70	19,917
Chemotherapy	44	4,299	56	5,447
No chemotherapy	62	29,151	38	17,828
Health care access*				
Median surgeon density† (IQR)	11 (8–16)		10 (6–15)	
Median radiation oncologist density‡ (IQR)	13 (4–20)		11 (0–19)	
Socioeconomic status*				
Living in metropolitan area	62	25,979	38	16,132
Living in nonmetropolitan area	51	7,193	49	6,971
Median income, $ (IQR)	41,691 (36,221–48,059)		39,879 (34,267–45,922)	
Median % living in poverty (IQR)	10.7 (8–14)		11.4 (9–14)	
Median % with college education (IQR)	24 (17–29)		22 (15–28)	

p values are < 0.001 for all data.
*By patient county of residence.
†Per 100,000 persons.
‡Per 10,000 persons.
BCS, breast-conserving surgery; IQR, interquartile range.

early-stage disease were more likely to undergo BCS. Patients who did not receive chemotherapy or did not undergo axillary surgery were also more likely to undergo BCS (Table 1). In addition, neighborhood socioeconomic factors were also highly associated with BCS. Specifically, patients living in metropolitan areas and in counties with higher median household income, lower percentage living below poverty level, and higher percentage with college education were more likely to undergo BCS. Of patients living in nonmetropolitan areas, only 51% underwent BCS. Supply of health-care providers also influenced treatment, with BCS use more likely in patients residing in counties with a higher density of surgeons and radiation oncologists (Table 1).

Finally, significant geographic variation existed ($p < 0.001$), with patients in the Northeast and Pacific West most likely to undergo BCS. In contrast, patients in the South were least likely to undergo BCS, with half or fewer of all patients in these regions treated with BCS (Fig. 1; Table 2). On adjusted analysis, higher density of surgeons was no longer a significant predictor of BCS use ($p = 0.13$), specifically, once the multivariate model accounted for geographic region. But a higher

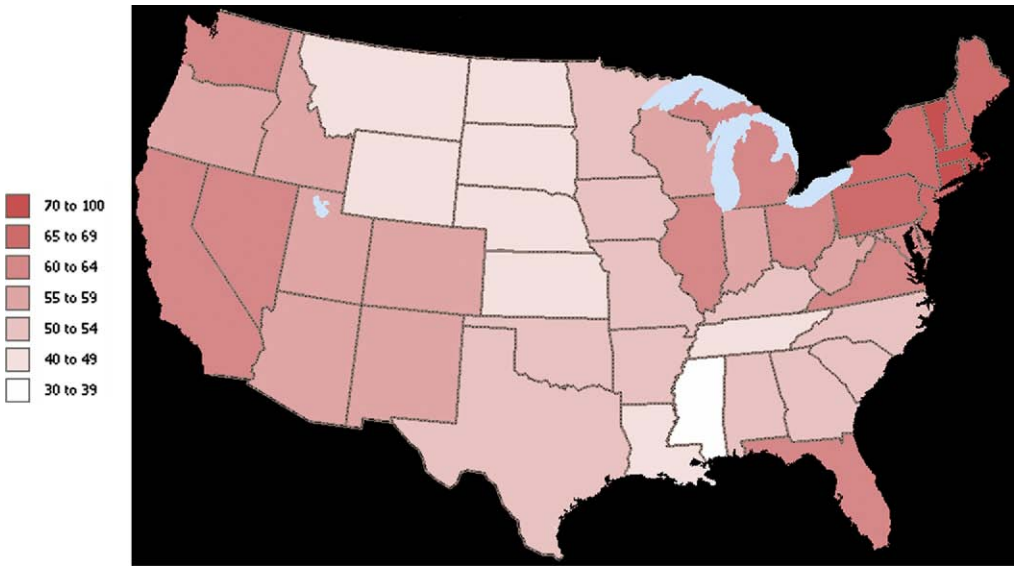

Figure 1. Percent use of breast-conserving surgery (BCS) by state. Darker shading represents higher frequency of use. Not shown: Alaska (55%) and Hawaii (67%).

density of radiation oncologists remained a significant predictor of BCS use ($p = 0.01$) (Table 3).

Early-stage breast cancer subgroup

In the selected subgroup of 43,706 patients with predicted early-stage (stage I or II) disease (77% of the entire sample), a total of 68% (29,828 of 43,706) of this selected group received BCS. This was consistent with a total of 65% (27,544 of 42,499) who received BCS in the validation subgroup of patients who did not have axillary involvement and did not receive chemotherapy. Geographic variation persisted in the use of BCS for patients with predicted early-stage disease. Patients in the Northeast (78% to 79%) and Pacific West (71%) were still the most likely to undergo BCS; patients in the South (57% to 59%) and portions of the Midwest (58%) were the least likely (Table 2). The validation subgroup was similar, with BCS ranging from 54% (South) to 75% (Northeast). On adjusted analysis, significant predictors of BCS use included similar demographic, clinical, and socioeconomic factors as predictors for the entire sample (Table 3). Significant predictors of BCS use identified in the validation group for early-stage breast cancer were also consistent with this analysis.

DISCUSSION

In this contemporary national cohort of older patients, we found that overall, a majority of surgically treated patients

Table 2. Unadjusted and Adjusted Percent Use of Breast-Conserving Surgery Versus Mastectomy by Geographic Region

		BCS, % (n = 23,275)			Mastectomy, % (n = 33,450)		
Region	**States**	**Overall**	**Adjusted***	**Early stage**	**Overall**	**Adjusted***	**Early stage**
West, Pacific West	AK, CA, HI, OR, WA	62	62	71	38	38	29
West, Mountain West	AZ, CO, ID, MT, NV, NM, UT, WY	57	58	66	43	42	34
Midwest, West North Central	IA, KS, MN, MO, NE, ND, SD	50	51	58	50	49	41
Midwest, East North Central	IL, IN, MI, OH, WI	61	60	70	39	40	30
Northeast, New England	CT, MA, NH, ME, RI, VT	70	63	79	30	36	21
Northeast, Mid-Atlantic	NJ, NY, PA	67	64	78	33	35	22
South, South Atlantic	DE, DC, FL, GA, MD, NC, SC, VA, WV	59	59	68	41	41	32
South, West South Central	AK, LA, OK, TX	50	54	59	50	45	41
South, East South Central	AL, KY, MS, TN	48	51	57	52	48	43

*Adjusted for covariates, including age, race, comorbidity score, axillary lymph node involvement, axillary dissection, chemotherapy, screening mammography, physician visits, surgeon density, radiation oncologist density, metropolitan area, poverty, and education.
BCS, breast-conserving surgery.

Table 3. Multivariate Logistic Model: Predictors of Use of Breast-Conserving Surgery

	Entire sample				Early-stage subgroup			
Covariate	**Odds ratio**	**95% CI**		**p Value**	**Odds ratio**	**95% CI**		**p Value**
Age 66 to < 70 y vs ≥ 70 y	1.37	1.31	1.44	< 0.001	1.15	1.09	1.22	< 0.001
Race								
Caucasian versus African American	1.14	1.05	1.23	< 0.001	0.95	0.86	1.04	0.26
Caucasian versus other race	1.29	1.15	1.45	< 0.001	1.17	1.08	1.27	< 0.001
Charlson comorbidity score								
0 versus 1 comorbid condition	1.18	1.13	1.24	< 0.001	1.21	1.15	1.28	< 0.001
0 versus 2 or more comorbid conditions	1.38	1.29	1.47	< 0.001	1.17	1.08	1.27	< 0.001
0 versus unknown comorbid conditions	1.12	1.01	1.25	0.03	0.91	0.79	1.05	0.20
Lymph node-negative disease	1.60	1.52	1.68	< 0.001	—	—	—	—
No axillary lymph node dissection*	4.00	3.85	4.17	< 0.001	4.65	4.46	4.88	< 0.001
No chemotherapy*	1.32	1.25	1.39	< 0.001	0.63	0.57	0.69	< 0.001
Screening mammography	2.02	1.87	2.17	< 0.001	0.89	0.80	1.00	0.04
One or more visits to physician	1.43	1.22	1.68	< 0.001	1.97	1.60	2.43	< 0.001
Geographic region†								
West, Pacific West	0.86	0.78	0.95	0.008	0.81	0.72	0.92	0.001
West, Mountain West	0.71	0.63	0.80	< 0.001	0.69	0.60	0.80	< 0.001
Midwest, West North Central	0.50	0.45	0.55	< 0.001	0.45	0.40	0.51	< 0.001
Midwest, East North Central	0.80	0.73	0.88	< 0.001	0.75	0.67	0.84	< 0.001
Northeast, Mid-Atlantic	1.05	0.95	1.16	0.34	1.06	0.94	1.19	0.36
South, South Atlantic	0.76	0.69	0.83	< 0.001	0.69	0.62	0.78	< 0.001
South, West South Central	0.58	0.53	0.65	< 0.001	0.54	0.48	0.61	< 0.001
South, East South Central	0.51	0.45	0.57	< 0.001	0.45	0.39	0.52	< 0.001
Surgeon density‡	1.00	0.99	1.01	0.13	1.00	0.99	1.01	0.14
Radiation oncologist density§	1.30	1.06	1.59	0.01	1.37	1.07	1.75	0.01
Living in metropolitan area	1.20	1.14	1.26	< 0.001	1.20	1.13	1.27	< 0.001
Percent living in poverty < 11%‖	1.05	1.00	1.09	0.03	1.05	1.00	1.11	0.06
Percent with college education > 23%‖	1.13	1.08	1.19	< 0.001	1.15	1.09	1.21	< 0.001

*A model excluding axillary lymph node dissection and chemotherapy, which are treatments likely to occur concurrently or after surgery, did not affect risk estimates for other covariates.
†Compared with reference category Northeast New England. The likelihood ratio test for all strata of the variable for region was statistically significant ($p < 0.001$).
‡Increased odds per 1 surgeon per 100,000 persons (continuous variable).
§Increased odds per 1 radiation oncologist per 10,000 persons (continuous variable).
‖Continuous variables dichotomized at the median value.

with invasive breast cancer received BCS rather than mastectomy: 59% of the entire sample and up to 68% of those with predicted early-stage disease. But we found considerable variations in BCS use by several important factors. First, clear regional differences existed. In some regions an exceptionally high percentage of patients received BCS (up to 79% in predicted early-stage patients in the Northeast), but only about half of patients in areas of the South received BCS. Second, neighborhood socioeconomic characteristics also appeared to influence BCS use, with the presence of county-level poverty and lower education levels both associated with lower use of BCS. Furthermore, health-care access also appeared to influence treatment patterns, with patients living in metropolitan areas and areas with a higher density of radiation oncologists more likely to receive BCS. Surgeon density did not appear to influence BCS versus mastectomy use.

Previous studies of patients treated in the 1980s and 1990s reported lower rates of BCS use compared with these more contemporary results. For example, in a similar cohort of Medicare patients diagnosed with invasive breast cancer in 1986, Nattinger and colleagues[7] reported only a 12% use of BCS just after the initial publication of the NSABP-B06 trial in 1985.[1,4,7] Subsequently, in 1990, a National Institutes of Health Consensus Development Conference statement declared that breast conservation was considered the preferred treatment choice for the majority of women with early-stage disease.[4] Since that time, steady increases have occurred in BCS use,[8,22] but studies have consistently found that the majority of patients with

invasive breast cancer in the US have been treated with mastectomy. For example, a more recent study by Morrow and associates[6] found that in 1994, BCS use was still only 43% in patients with stage I or stage II breast cancer across the US. Continued evidence has accumulated, providing increasingly convincing data that BCS plus radiotherapy is comparable to mastectomy in early-stage patients, including the 20-year followup of the NSABP-B06 trial published in 2002,[2,3] demonstrating low local failure rates after breast conservation. With this published data it is not surprising that the overall frequency of BCS in our more recent cohort demonstrates continued increases in use. Future studies may seek to determine how trends in mastectomy versus BCS continue to evolve. Recent data suggest a reversal in use trends may be occurring, with an increasing number of patients receiving mastectomy, potentially influenced by changing technologies in breast cancer care, such as the use of breast MRI.[23] Alternatively, the convenience of other emerging technologies, such as accelerated partial breast irradiation and hypofractionated whole breast irradiation, may increase the frequency of breast conservation.

Substantial geographic variation in BCS use also existed in earlier treatment eras, with a nearly identical pattern to that found in our study. Patients in the northeastern regions of the US have consistently been the most likely to receive BCS and those in southern regions the least likely, and this pattern has persisted over approximately the last two decades.[6,7,24,25] Several potential causes for this marked variation have been studied. First, physician influences on surgical treatment choices have been considered. Various surgeon characteristics have been found to influence the use of BCS versus mastectomy, including surgeon gender, practice setting, geographic setting (rural versus urban), and practice volume.[26-28] Other surgeon characteristics, including surgical or educational background and surgical experience, have been found to influence other aspects of treatment, such as receipt of radiotherapy and use of sentinel lymph node biopsy.[29,30] In addition, patient preferences and the patient-surgeon interaction influence surgical treatment choice. Several earlier studies have noted that even when offered or recommended the option of breast-conserving therapy, some patients still choose mastectomy.[31] Accordingly, treatment goals should account for individual, regional, or cultural preferences for care.

Finally, previous studies of patients treated in earlier eras demonstrated that socioeconomic factors, such as non-Caucasian race, lower income, higher poverty levels, and lower education, were significant barriers to receipt of BCS.[32] Our analysis of the early-stage disease subgroup suggests that racial differences in treatment for African-American patients and Caucasian patients may have decreased compared with those reported in earlier studies.[8] Unfortunately, the persistent finding of the other socioeconomic barriers in our contemporary cohort suggest that little progress has been made in overcoming disparities in the use of breast-conserving therapy, particularly for patients living in the most disadvantaged neighborhoods and regions. Indeed, initiation and completion of radiotherapy after BCS itself has been found in earlier studies to vary with socioeconomic factors.[33,34] So, strategies to improve access to radiotherapy[35] may also serve as important factors in promoting BCS, especially in patients who would prefer this surgical treatment modality. Notably, a unique finding of our study was that the supply of radiation oncologists (as measured by the density of radiation oncologist by county) was a major factor affecting the choice to pursue BCS. Other than geographic region, this socioeconomic variable had the largest effect size for association with surgical treatment choice. Previous studies have noted that increased distance from radiation oncologists is a barrier to treatment with BCS.[35,36] Similarly, our result supports the hypothesis that access to radiation oncologists continues to be an important factor, which may affect decision making by both patients and physicians regarding surgical treatment.

Limitations

Our study has several limitations to consider. Our sample focused on older breast cancer patients with continuous fee-for-service Medicare Part A and B insurance coverage. So, future studies will be required to validate the magnitude and significance of predictors of BCS use in younger patients. In addition, studies are also needed to determine the magnitude of potential disparities in use among patients with other insurance status, given that earlier evidence suggests that insurance status may influence surgical treatment strategies.[32] Misclassification of the outcome, surgical treatment, was possible, given that this variable was claims based. We excluded the very small percentage (1%) of patients who had both claims for BCS and mastectomy, but mastectomy did not appear to be the definitive operation (mastectomy preceded BCS or occurred more than 3 months after BCS) in order to reduce this potential source of misclassification. Additionally, in our subsidiary analysis, claims-based algorithms were used as a proxy for early-stage disease, so sensitivity and specificity of the definitions were not 100%. Because early-stage disease is an important determinant of whether BCS is a surgical treatment choice, it is likely that the true frequency of BCS use lies between 59% and 68%. So future studies may seek to validate and refine the estimated frequency of BCS use in patients with confirmed early-stage disease. Finally, although our multi-

variate model adjusted for a large number of covariates, residual confounding may still exist, so our model may not be able to distinguish exactly the contribution of physician, patient, geographic, and socioeconomic factors to treatment decisions. Our large, national, retrospective cohort-based dataset serves as an important complement to other studies that have more detailed data on the interactions between patients and physicians and patients and socioeconomic factors.[31]

In conclusion, in this contemporary study we demonstrated that currently more than half of older women across the US diagnosed with nonmetastatic invasive breast cancer are treated with BCS. This represents substantially increased use rates compared with historical data. Yet marked variation across the US persists in BCS use. Lack of BCS use appears to be associated with socioeconomic disadvantage, suggesting that persistent barriers to breast conservation exist.

Author Contributions

Study conception and design: GL Smith, Buchholz
Acquisition of data: GL Smith, Shih, Giordano, Buchholz
Analysis and interpretation of data: GL Smith, Xu, Shih, Giordano, BD Smith, Hunt, Strom, Perkins, Hortobagyi, Buchholz
Drafting of manuscript: GL Smith
Critical revision: Xu, Shih, Giordano, BD Smith, Hunt, Strom, Perkins, Hortobagyi, Buchholz

REFERENCES

1. Fisher B, Bauer M, Margolese R, et al. Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer. N Engl J Med 1985;312:665–673.
2. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002;347:1233–1241.
3. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 2002;347:1227–1232.
4. Consensus statement: treatment of early-stage breast cancer. National Institutes of Health Consensus Development Panel. J Natl Cancer Inst Monogr 1992:15.
5. Morrow M. Rational local therapy for breast cancer. N Engl J Med 2002;347:1270–1271.
6. Morrow M, White J, Moughan J, et al. Factors predicting the use of breast-conserving therapy in stage I and II breast carcinoma. J Clin Oncol 2001;19:2254–2262.
7. Nattinger AB, Gottlieb MS, Veum J, et al. Geographic variation in the use of breast-conserving treatment for breast cancer. N Engl J Med 1992;326:1102–1107.
8. Gilligan MA, Kneusel RT, Hoffmann RG, et al. Persistent differences in sociodemographic determinants of breast conserving treatment despite overall increased adoption. Med Care 2002;40:181–189.
9. Michalski TA, Nattinger AB. The influence of black race and socioeconomic status on the use of breast-conserving surgery for Medicare beneficiaries. Cancer 1997;79:314–319.
10. National Cancer Institute. SEER-Medicare linked database. Available at: http://healthservices.cancer.gov/seermedicare/. Accessed June 25, 2009.
11. Nattinger AB, Laud PW, Bajorunaite R, et al. An algorithm for the use of Medicare claims data to identify women with incident breast cancer. Health Serv Res 2004;39:1733–1749.
12. Gold HT, Do HT. Evaluation of three algorithms to identify incident breast cancer in Medicare claims data. Health Serv Res 2007;42:2056–2069.
13. Smith BD, Gross CP, Smith GL, et al. Effectiveness of radiation therapy for older women with early breast cancer. J Natl Cancer Inst 2006;98:681–690.
14. Smith BD, Haffty BG, Buchholz TA, et al. Effectiveness of radiation therapy in older women with ductal carcinoma in situ. J Natl Cancer Inst 2006;98:1302–1310.
15. Smith BD, Haffty BG, Smith GL, et al. Use of postmastectomy radiotherapy in older women. Int J Radiat Oncol Biol Phys 2008;71:98–106.
16. Smith BD, Smith GL, Buchholz TA. Controversies over the role of radiation therapy for ductal carcinoma in situ. Expert Rev Anticancer Ther 2008;8:433–441.
17. Smith BD, Smith GL, Haffty BG. Postmastectomy radiation and mortality in women with T1–2 node–positive breast cancer. J Clin Oncol 2005;23:1409–1419.
18. Smith GL, Smith BD, Giordano SH, et al. Risk of hypothyroidism in older breast cancer patients treated with radiation. Cancer 2008;112:1371–1379.
19. Klabunde CN, Potosky AL, Legler JM, Warren JL. Development of a comorbidity index using physician claims data. J Clin Epidemiol 2000;53:1258–1267.
20. US Census Bureau. Available at: http://www.census.gov. Accessed June 25, 2009.
21. Health Resources and Services Administration. Area Resource File. Available at: http://www.arfsys.com/overview.htm. Accessed June 25, 2009.
22. Freedman RA, He Y, Winer EP, Keating NL. Trends in racial and age disparities in definitive local therapy of early-stage breast cancer. J Clin Oncol 2009;27:713–719.
23. Katipamula R, Hoskin TL, Boughey JC, et al. Trends in mastectomy rates at the Mayo Clinic Rochester: effect of surgical year and pre-operative MRI. Proceedings from the 44th annual meeting of the American Society of Clinical Oncology. Chicago, IL, Abstract #509, 2008.
24. Kelemen JJ 3rd, Poulton T, Swartz MT, Jatoi I. Surgical treatment of early-stage breast cancer in the Department of Defense Healthcare System. J Am Coll Surg 2001;192:293–297.
25. Chagpar AB, Studts JL, Scoggins CR, et al. Factors associated with surgical options for breast carcinoma. Cancer 2006;106:1462–1466.
26. Gilligan MA, Neuner J, Sparapani R, et al. Surgeon characteristics and variations in treatment for early-stage breast cancer. Arch Surg 2007;142:17–22.
27. Hokanson P, Seshadri R, Miller KD. Underutilization of breast-conserving therapy in a predominantly rural population: need

for improved surgeon and public education. Clin Breast Cancer 2000;1:72–76.
28. Neuner JM, Gilligan MA, Sparapani R, et al. Decentralization of breast cancer surgery in the United States. Cancer 2004;101: 1323–1329.
29. Hershman DL, Buono D, McBride RB, et al. Surgeon characteristics and receipt of adjuvant radiotherapy in women with breast cancer. J Natl Cancer Inst 2008;100:199–206.
30. Hutchinson JR, Chagpar AB, Scoggins CR, et al. Surgeon and community factors affecting breast cancer sentinel lymph node biopsy. Am J Surg 2005;190:903–906.
31. Katz SJ, Lantz PM, Janz NK, et al. Patient involvement in surgery treatment decisions for breast cancer. J Clin Oncol 2005; 23:5526–5533.
32. McCarthy EP, Ngo LH, Roetzheim RG, et al. Disparities in breast cancer treatment and survival for women with disabilities. Ann Intern Med 2006;145:637–645.
33. Smith G, Shih Y, Xu Y, et al. Racial disparities in radiation therapy following breast conserving surgery: a national Medicare study. Accepted for publication Cancer, 2009.
34. Srokowski TP, Fang S, Duan Z, et al. Completion of adjuvant radiation therapy among women with breast cancer. Cancer 2008;113:22–29.
35. Baldwin LM, Taplin SH, Friedman H, Moe R. Access to multidisciplinary cancer care: is it linked to the use of breast-conserving surgery with radiation for early-stage breast carcinoma? Cancer 2004;100:701–709.
36. Voti L, Richardson LC, Reis IM, et al. Treatment of local breast carcinoma in Florida: the role of the distance to radiation therapy facilities. Cancer 2006;106:201–207.

Appendix. Covariates and Associated Claims Codes Derived from Medicare Files

Predictor variable	Time period searched	Source file	ICD-9 diagnosis	ICD-9 procedure	CPT	Revenue center
Demographic						
Age	At diagnosis	Denominator				
Race	At diagnosis	Denominator				
Extent of disease at diagnosis						
Axillary LN involvement	3 mo before to 3 mo after		1963			
Metastatic disease	3 mo before to 3 mo after		1962, 1965–6, 197, 1970, 1971, 1972, 1973, 1974, 1975, 1976, 1977, 1978, 198, 1980, 1981, 1982, 1983, 1984, 1985, 1986, 1987, 1988, 19881, 19882, 19889			
Cancer treatment						
No. visits to surgeon	In the year after diagnosis	Carrier claims				
No. visits to medical oncologist	In the year after diagnosis	Carrier claims				
No. visits to radiation oncologist	In the year after diagnosis	Carrier claims				
Imaging (CT, MRI, PET, or bone scan)	In the 3 mo after diagnosis			8801, 8703, 8741, 8891, 8896, 8874, 9218, 9214	70450, 70460, 70470, 70551–3, 71250, 71260, 71270, 72192–4, 74150, 74160, 74170, 76700, 78315, 78320, 78812–6, G0213–5	
Radiation therapy	In the 9 mo after diagnosis		V580, V661, V671	9221–7, 9229	77401–77525, 77761–77799	0330, 0333
Breast-conserving surgery	In the 9 mo after diagnosis			8520–3, 8525	19110, 19120, 19125, 19160, 19162	
Mastectomy	In the 9 mo after diagnosis			8541–8	19180, 19182, 19200, 19220, 19240	
Axillary LN dissection	3 mo before to 1 y after			4023, 4051, 8543, 8547	38740, 38745, 19162, 19200, 19220, 19240	
Chemotherapy (any agent)	In the 9 mo after diagnosis		V581, V662, V672	9925	96400–96549, J9000–9, Q0083–5	0331, 0332, 0335
Doxorubicin					J9000–1, J9180	
Paclitaxel					J9170, J9265	

(continued)

Appendix. Continued

Predictor variable	Time period searched	Source file	ICD-9 diagnosis	ICD-9 procedure	CPT	Revenue center
Preventive care and interaction with health care system						
No. physician visits	In the y before diagnosis	All				
Screening ammography	In the y before diagnosis		V7611, V7612	8737, 8736	77055–6, 77058–9, 76090–2, G0202, G0204, G0206	0401, 0403
Influenza vaccine	In the y before diagnosis		V0481		90658, G0008	
General health status						
Any hospital admission	In the y after diagnosis	Inpatient				
Charlson comorbidity score	In the y before diagnosis up to 1 mo after diagnosis	Per prior studies*				

*Klabunde CN, Potosky AL, Legler JM, Warren JL. Development of a comorbidity index using physician claims data. J Clin Epidemiol 2000;53:1258–1267.
CPT, Common Procedural Terminology; LN, lymph node; PET, positron emission tomography.

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ORIGINAL REPORT

Brachytherapy for Accelerated Partial-Breast Irradiation: A Rapidly Emerging Technology in Breast Cancer Care

Grace L. Smith, Ying Xu, Thomas A. Buchholz, Benjamin D. Smith, Sharon H. Giordano, Bruce G. Haffty, Frank A. Vicini, Julia R. White, Douglas W. Arthur, Jay R. Harris, and Ya-Chen T. Shih

From The University of Texas MD Anderson Cancer Center, Houston, TX; University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, New Brunswick, NJ; William Beaumont Hospital, Royal Oak, MI; Medical College of Wisconsin, Milwaukee, WI; Virginia Commonwealth University, Richmond, VA; and Dana-Farber Cancer Institute, Brigham and Women's Hospital, Boston, MA.

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Corresponding author: Ya-Chen T. Shih, PhD, Section of Health Services Research, Department of Biostatistics, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, PO Box 301402, Houston, TX 77030; e-mail: yashih@mdanderson.org.

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ABSTRACT

Purpose
Brachytherapy is a method for delivering partial-breast irradiation after breast-conserving surgery (BCS). It is currently used in the community setting, although its efficacy has yet to be validated in prospective comparative trials. Frequency and factors influencing use have not been previously identified.

Methods
In a nationwide database of 6,882 Medicare beneficiaries (age ≥ 65 years) with private supplemental insurance (MarketScan Medicare Supplemental), claims codes identified patients treated with brachytherapy versus external-beam radiation after BCS for incident breast cancer (diagnosed from 2001 to 2006). Logistic regression modeled predictors of brachytherapy use.

Results
Frequency of brachytherapy use as an alternative to external-beam radiation after BCS increased over time (< 1% in 2001, 2% in 2002, 3% in 2003, 5% in 2004, 8% in 2005, 10% in 2006; $P < .001$). Increased use correlated temporally with US Food and Drug Administration approval and Medicare reimbursement of brachytherapy technology. Brachytherapy use was more likely in women with lymph node–negative disease (odds ratio [OR], 2.19; 95% CI, 1.17 to 4.11) or axillary surgery (OR, 1.74; 95% CI, 1.23 to 2.44). Brachytherapy use was also more likely in women with non–health maintenance organization insurance (OR, 1.81; 95% CI, 1.24 to 2.64) and in areas with higher median income (OR, 1.58; 95% CI, 1.05 to 2.38), lower density of radiation oncologists (OR, 1.78; 95% CI, 1.11 to 2.86), or higher density of surgeons (OR, 1.57; 95% CI, 1.07 to 2.31).

Conclusion
Despite ongoing questions regarding efficacy, breast brachytherapy was rapidly incorporated into the care of older, insured patients. In our era of frequently emerging novel technologies yet growing demands to optimize costs and outcomes, results provide insight into how clinical, policy, and socioeconomic factors influence new technology diffusion into conventional care.

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INTRODUCTION

Brachytherapy is a radiation treatment administered through local implantation of a radioactive source. In recent years, brachytherapy has emerged as an important technique for the delivery of partial-breast irradiation after breast-conserving surgery (BCS), particularly in selected patients with breast cancer with low-risk features such as smaller tumor size and node-negative disease. In these patients, either multiple interstitial catheters or a single balloon catheter are placed, allowing the radiation treatment to be delivered locally to tissue at the highest risk for recurrence. Compared with a standard course of external-beam radiation therapy (EBRT) to the whole breast, a brachytherapy course is typically several weeks shorter, thereby reducing inconvenience associated with radiation treatment.

However, the use of breast brachytherapy as the sole radiation treatment after BCS remains controversial. EBRT to the whole breast after BCS is widely accepted as the definitive standard therapy for early-stage disease based on extensive randomized studies. Data have accumulated demonstrating local control and survival benefits attributable to EBRT over follow-up as long as 20 years.[1-4] In contrast, phase III trials directly comparing breast brachytherapy with standard EBRT after BCS have yet to mature.[5] Moreover, existing phase II studies of breast brachytherapy have generally included relatively small sample sizes and have limited median follow-up times, typically around 3 to 5 years.[6-12]

Although it seems that, in the community (nonclinical trial) setting, there is ongoing use of breast brachytherapy after BCS, the actual frequency of utilization is unknown. Additionally, the factors influencing its use have not been previously studied. The lack of studies on breast brachytherapy utilization patterns is surprising, given that substantial controversy exists over its current use in the community setting. Specifically, some experts consider this treatment strategy still unproven because of the existing gaps in the scientific literature regarding its efficacy.[13] Furthermore, others considered this strategy one of the costlier options for patients with candidate low-risk tumors treated in the era of its initial diffusion.[14]

Documenting the pattern by which this novel—but also potentially unproven and costly—treatment has diffused into the care of patients with breast cancer across the United States offers a unique opportunity to help clinicians and policy makers better understand how clinical factors, policy factors, and socioeconomic factors influence the dissemination of new technologies into the health care system. Therefore, in a national cohort of older, insured patients diagnosed with invasive breast cancer, we sought to quantify the frequency of breast brachytherapy utilization, identify time trends in breast brachytherapy use, and identify clinical and nonclinical factors associated with brachytherapy use.

METHODS

Data Set and Study Sample

The MarketScan Medicare Supplemental database is a large, nationwide, employment-based claims database that includes Medicare beneficiaries with private supplemental insurance (Appendix Table A1, online only).[15] During the study interval, approximately two thirds of Medicare beneficiaries had private supplemental insurance. The University of Texas M. D. Anderson Cancer Center's Institutional Review Board exempted this study for approval because all patient data were de-identified.

We developed an algorithm to identify patients with incident breast cancer treated with BCS. Our method was based on a prior validated algorithm for claims data.[16,17] Our initial study population consisted of 23,576 women who had any diagnosis claims code indicating invasive breast cancer (defined as International Classification of Diseases, Ninth Revision diagnosis code of 174) plus a procedure code related to breast cancer (Appendix, online only) during the study period (2001 to 2006). The earliest date with a diagnosis or procedure code indicative of breast cancer was considered the index date (a proxy measure for the diagnosis date). After applying criteria to exclude prevalent cases, patients younger than age 65 years at diagnosis, men, and patients with incomplete treatment course information (see Appendix for expanded algorithm), our final sample included 6,882 women.

Radiation Therapy and Other Covariates

Patients were classified as treated with any radiation therapy if a diagnosis or procedure claim was recorded within 6 months of the index claim date. Of those, patients were further classified as treated with EBRT, brachytherapy, or both (EBRT plus brachytherapy boost), as indicated by claims codes. Patients treated with brachytherapy were further classified as having received balloon-based treatment if a procedure code was found specifying that procedure (Appendix 1).

Other clinical variables were defined using claims-based criteria and were used as covariates. A complete list of variables is provided in the Appendix. Definitions of the clinical variables were derived from claims-based definitions used in prior studies of patients with breast cancer.[18] Published clinical guidelines on the use of breast brachytherapy offer recommendations based on age, tumor size, extent, histology, multicentricity, receptor status, and surgical history.[19-21] Of these variables, only extent (presence of lymph node involvement or metastatic disease) and surgical history were available in our data set to be evaluated. Other covariates included in our analysis were demographic variables and socioeconomic variables, listed in detail in the Appendix. For univariate and multivariate analyses, continuous variables were categorized into quartiles a priori.

Statistical Analysis

All analyses were conducted using SAS software version 9.1.3 (SAS Institute, Cary, NC), and all statistical tests assumed a two-tailed $\alpha = .05$. To address our first objective, we calculated percent use of brachytherapy, EBRT, and EBRT plus brachytherapy boost for the entire sample and by year of diagnosis. To address our second objective, we evaluated for a time trend using the Mantel-Haenszel χ^2 and Cochran-Armitage tests for trend.[22] We also benchmarked the time trends against the following two major policy events that occurred during the study period: US Food and Drug Administration (FDA) approval of the first balloon-based brachytherapy device for breast cancer in June 2002 and Medicare reimbursement of breast brachytherapy in April 2004.

Because our third objective was to understand the clinical and nonclinical factors influencing selection of brachytherapy alone versus conventional EBRT and because the number of patients who used EBRT plus brachytherapy boost was small, we excluded 28 patients who received EBRT plus brachytherapy boost from the denominator for subsequent analyses. In addition, because few patients received brachytherapy alone before 2003, 1,505 patients treated before 2003 were excluded from analyses designed to address our third objective, for a total of 5,349 included patients. Multivariate analyses on this group included 5,031 patients with complete covariate information.

To address our third objective, we tested univariate and multivariate associations, with the outcome variable dichotomized as receipt of brachytherapy alone versus EBRT. The univariate associations between this outcome and clinical, demographic, and socioeconomic covariates were assessed using the Pearson χ^2 test for categorical variables and the Wilcoxon rank sum test for continuous variables. Multivariate logistic models tested adjusted associations (Appendix).[22,23]

RESULTS

Patient Characteristics

Of 6,882 women treated with BCS and radiation treatment, the mean age was 75 years (standard deviation, 6 years). Eight percent of women had axillary involvement, and 4% had metastatic disease at diagnosis. Seventy-eight percent of women underwent any axillary surgery, 10% received chemotherapy, and 65% received endocrine therapy as part of the initial treatment course.

Frequency of Brachytherapy and EBRT Use and Temporal Trends

Of the entire sample, 333 (5%) of 6,882 women received brachytherapy alone (multicatheter or balloon-based), 6,521 (95%) of 6,882 women received EBRT, and 28 (< 1%) of 6,865 women received EBRT plus brachytherapy boost. Treatments with brachytherapy alone significantly increased over time, from less than 1% in 2001, 2% in 2002, 3% in 2003, 5% in 2004, 8% in 2005, and 10% in 2006 ($P < .001$; Table 1). The most notable increases could be benchmarked against two major policy events. First, an increase in use was noted after July 2002, correlating with FDA approval of the balloon-based breast brachytherapy device (June 2002). Second, a further increase was noted after July 2004, correlating with Medicare reimbursement of treatment (April 2004; Fig 1). Of patients treated with any form of brachytherapy alone, the proportion who received balloon-based treatment also increased dramatically over time, with

Table 1. Temporal Trends: Patients Receiving EBRT Alone, EBRT Plus Brachytherapy Boost, or Brachytherapy Alone During the Study Period ($P < .001$)

Time Period	Total No. of Patients	Patients Receiving EBRT Alone		Patients Receiving EBRT + Boost		Patients Receiving Brachytherapy Alone	
		No.	%	No.	%	No.	%
1/1/2001 to 6/30/2001	183	181	98.91	0	0.00	2	1.09
7/1/2001 to 12/30/2001	363	359	98.90	2	0.55	2	0.55
1/1/2002 to 6/30/2002	469	466	99.36	1	0.21	2	0.43
7/1/2002 to 12/30/2002	494	478	96.76	1	0.20	15	3.04
1/1/2003 to 6/30/2003	711	691	97.19	1	0.14	19	2.67
7/1/2003 to 12/30/2003	828	796	96.14	4	0.48	28	3.38
1/1/2004 to 6/30/2004	874	827	94.62	3	0.34	44	5.03
7/1/2004 to 12/30/2004	851	804	94.48	2	0.24	45	5.29
1/1/2005 to 6/30/2005	942	865	91.83	8	0.85	69	7.32
7/1/2005 to 12/30/2005	534	489	91.57	2	0.37	43	8.05
1/1/2006 to 6/30/2006	633	565	89.26	4	0.63	64	10.11
Total	6,882	6,521	94.75	28	0.41	333	4.83

Abbreviation: EBRT, external-beam radiation therapy.

89% receiving balloon-based treatment by 2006 (Fig 2). In multivariate analysis, the temporal trend indicating a steady increase in the use of brachytherapy remained significant ($P < .001$; Table 2).

Clinical Predictors of Treatment With Brachytherapy Alone

In multivariate analysis, treatment with brachytherapy alone was also associated with multiple clinical factors. Brachytherapy alone was more likely in women who had lymph node–negative disease (odds ratio [OR], 2.19; 95% CI, 1.17 to 4.11), did not receive chemotherapy (OR, 1.68; 95% CI, 1.01 to 2.80), and received any axillary surgery (OR, 1.74; 95% CI, 1.23 to 2.44; Tables 2 and 3). Reassuringly, only 2% of patients with metastatic disease and 3% of patients with axillary nodal involvement received brachytherapy alone.

Nonclinical Predictors of Treatment With Brachytherapy Alone

Several nonclinical factors were significant predictors of treatment. Geographic region was a strong predictor of treatment with brachytherapy alone. Patients residing in the Northeast were less likely to receive brachytherapy alone, particularly compared with patients residing in the West and South (Tables 2 and 3). Second, health care access as reflected by type of private supplemental insurance was also a significant predictor. Brachytherapy alone was more likely in women whose supplemental insurance was non-HMO (OR, 1.81; 95% CI, 1.24 to 2.64).

Finally, several neighborhood socioeconomic factors marginally influenced treatment. Brachytherapy alone was more likely for patients living in areas with a higher median income (OR, 1.58; 95% CI, 1.05 to 2.38 for the second quartile compared with the lowest quartile) and in areas with a lower density of radiation oncologists (OR, 1.78; 95% CI, 1.11 to 2.86 for the second quartile compared with the lowest quartile). However, these comparisons were not significant for higher quartiles. In addition, in the provider-based model (socioeconomic variables were defined based on provider county), brachytherapy alone was more likely for patients who received their BCS in areas with the highest quartile density of surgeons (OR, 1.60; 95% CI, 1.09 to 2.34 for the highest quartile density compared with the lowest quartile

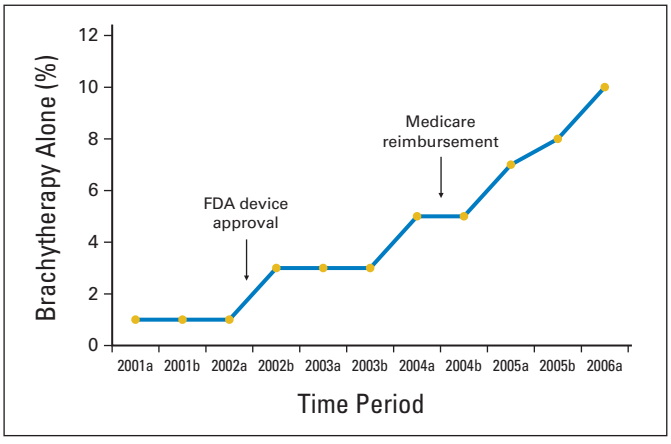

Fig 1. Temporal trends: percentage of patients treated with brachytherapy (multicatheter or balloon based) as the sole modality of radiotherapy after breast-conserving therapy ($P < .001$). The "a" after year refers to January through June, and "b" refers to July through December. FDA, US Food and Drug Administration.

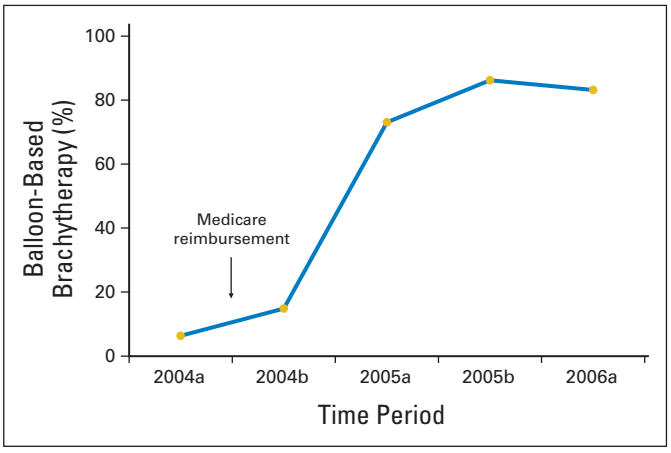

Fig 2. Temporal trends: percentage of patients treated with brachytherapy as the sole modality of radiotherapy after breast-conserving therapy who received balloon-based brachytherapy ($P < .001$). The "a" after year refers to January through June, and "b" refers to July through December.

Table 2. Multivariate Logistic Model: Adjusted OR for Predictors of Use of Brachytherapy Alone Versus EBRT Alone in the Study Period From 2003 to 2006 (N = 5,031)

Predictor Variable	Patient-Based Model*		
	OR	95% CI	*P*
Age, years			
< 70	1.00†		
70-79	0.77	0.57 to 1.03	.08
≥ 80	1.08	0.76 to 1.54	.65
Employee relationship			
Employee	1.00		
Spouse	1.12	0.85 to 1.46	.42
Geographic region			
Northeast (reference group)	1.00		
West	2.69	1.46 to 4.93	.0010
Midwest	1.64	0.93 to 2.91	.09
South	2.39	1.33 to 4.30	.004
Charlson comorbidity score			
0	1.00		
≥ 1	1.14	0.68 to 1.90	.62
Any inpatient admission			
Yes	1.00		
No	0.87	0.44 to 1.69	.68
No. of outpatient physician visits	1.01	0.98 to 1.04	.62
Screening mammography			
Yes	1.00		
No	0.70	0.44 to 1.11	.13
Axillary lymph node involvement			
Yes	1.00		
No	2.18	1.17 to 4.10	.02
Metastatic disease			
Yes	1.00		
No	1.30	0.60 to 2.84	.51
Any axillary surgery			
No	1.00		
Yes	1.73	1.23 to 2.44	.002
Chemotherapy			
Yes	1.00		
No	1.67	1.01 to 2.79	.05
Endocrine therapy			
Yes	1.00		
No	0.93	0.72 to 1.21	.60
Insurance type			
HMO	1.00		
Non-HMO	1.80	1.23 to 2.62	.002
Surgeon density*‡			
Q1 (≤ 8)	1.00		
Q2 (9-11)	0.97	0.65 to 1.46	.90
Q3 (12-15)	0.91	0.57 to 1.45	.68
Q4 (> 15)	1.39	0.83 to 2.33	.21
Radiation oncologist density			
Q4 (> 19)	1.00		
Q1 (≤ 8)	1.78	1.10 to 2.86	.02
Q2 (9-13)	1.28	0.83 to 1.96	.26
Q3 (14-19)	0.91	0.61 to 1.35	.65
Metropolitan area			
No (reference group)	1.00		
Yes	1.30	0.80 to 2.13	.29
Median income,$			
Q1 (≤ 40,305)	1.00		
Q2 (40,306-45,290)	1.51	1.00 to 2.28	.05
Q3 (45,291-52,936)	1.39	0.84 to 2.31	.20
Q4 (> 52,936)	1.69	0.86 to 3.32	.13

(continued on following page)

Table 2. Multivariate Logistic Model: Adjusted OR for Predictors of Use of Brachytherapy Alone Versus EBRT Alone in the Study Period From 2003 to 2006 (N = 5,031) (continued)

Predictor Variable	Patient-Based Model*		
	OR	95% CI	*P*
Percentage living in poverty			
Q1 (≤ 9.3)	1.00		
Q2 (9.4-11.8)	0.96	0.64 to 1.44	.83
Q3 (11.9-15.2)	1.45	0.89 to 2.35	.14
Q4 (> 15.2)	1.32	0.75 to 2.32	.34
Percentage with college education or more			
Q1 (≤ 17.2)			
Q2 (17.3-24.9)	0.86	0.56 to 1.30	.47
Q3 (25.0-29.5)	1.46	0.93 to 2.30	.10
Q4 (> 29.5)	1.12	0.64 to 1.98	.69
Time period of treatment			
Before 7/1/2004 (reference group)	1.00		
7/1/2004 to 12/31/2004	1.58	1.08 to 2.30	.02
1/1/2005 to 6/30/2005	2.02	1.43 to 2.86	< .001
7/1/2005 to 12/31/2005	2.01	1.32 to 3.04	.001
1/1/2006 to 6/30/2006	2.60	1.81 to 3.76	< .001

Abbreviations: OR, odds ratio; EBRT, external-beam radiation therapy; HMO, health maintenance organization; Q quartile.
*By patient county of residence.
†An OR of 1.00 indicates the reference group.
‡Per 1000,000 persons.

density), although this difference was not significant for other quartile comparisons (Table 2).

DISCUSSION

To our knowledge, our analysis is the first to detail frequency and patterns of breast brachytherapy use in a nonclinical trial setting in the United States and, further, to identify potential clinical, policy, and socioeconomic influences on treatment utilization in older, well-insured women. In our cohort of older insured women diagnosed with breast cancer, we found that 5% of patients received brachytherapy as the sole radiotherapy modality after BCS during the study period. More importantly, our results demonstrated that in recent years, the use of brachytherapy alone after BCS increased significantly. By 2006, a substantial percentage of our cohort—as much as 10%—was treated with this modality, with the vast majority of this group using a balloon-based delivery system. Temporal trends found in our study could be benchmarked both against FDA approval of the balloon-based brachytherapy device for breast cancer and Medicare reimbursement of breast brachytherapy. Interestingly, FDA approval was directed at the brachytherapy balloon device only and thus did not evaluate clinical efficacy data (unlike FDA approval policy for pharmaceutical agents). However, the temporal correlation found in our study still suggests a potential influence of device approval policy, independent of accrual of clinical evidence. However, given that this correlation does not necessarily imply causation, the effect of approval policy on treatment selection may merit further investigation.

To our knowledge, no prior studies of breast brachytherapy have reported the frequency of its use in the community setting. The majority of published studies have occurred in the clinical trial setting, generally limited to select patients who meet criteria for lower risk tumors.[6] In contrast, our study provides new data to suggest that the use of breast brachytherapy, and particularly balloon-based techniques, is being incorporated both rapidly and extensively into treatment after BCS. In a recent study, an estimated 13% to 27% of patients treated with BCS were considered potential candidates for breast brachytherapy.[24] Thus, our results suggest that a substantial proportion of available candidate patients are currently being treated with this new technology. This increasing utilization may reflect, in part, a growing interest by both patients and providers in the convenience of accelerated partial-breast irradiation techniques. For breast brachytherapy, the typical treatment course is shortened by 4 to 6 weeks compared with standard EBRT to the whole breast, thus reducing the inconvenience of a long course of therapy. Alternatively, increasing utilization could have reflected a response to financial incentives for providers, with potentially higher reimbursements for this technology during the study period.

The relatively high frequency of use and the temporal trends indicating a rapid diffusion of this technology reported in our study are particularly noteworthy in the context of unanswered questions that remain regarding the most appropriate use of breast brachytherapy. In particular, the long-term efficacy of breast brachytherapy alone after BCS, specifically in comparison with standard treatment with EBRT to the whole breast, remains unclear. Only a small total number of patients have been accrued in randomized clinical studies evaluating the efficacy of all accelerated partial-breast irradiation techniques including brachytherapy, yielding approximately 1,500 patient-years of follow-up.[6,25] In comparison, cumulative data from randomized trials evaluating the added benefit of EBRT to the whole breast after BCS have accumulated approximately 60,000 to 100,000 patient-years of follow-up and

Table 3. Univariate Associations: Predictors of Use of Brachytherapy Alone Versus EBRT Alone in the Study Period From 2003 to 2006

Variable	Brachytherapy Alone (n = 294)		EBRT Alone (n = 4,737)		*P*
	No. of Patients	%	No. of Patients	%	
Demographic					
Age, years					
Mean	74		75		.25
SD	6		6		
< 70	79	6.7	1,098	93.4	.03
70-79	142	5.1	2,631	94.9	
≥ 80	73	6.9	1,008	93.1	
Employee relationship					.17
Employee	180	5.5	3,091	94.5	
Spouse	114	6.0	1,646	93.5	
Geographic region					.03
Northeast	15	3.3	437	96.7	
West	103	6.1	1,595	93.9	
Midwest	97	5.5	1,676	94.5	
South	79	7.1	1,029	92.9	
Clinical					
Charlson comorbidity score					.43
0	275	5.8	4,479	94.2	
≥ 1	19	6.9	258	93.1	
Any inpatient admission					.48
No	283	5.8	4,593	94.2	
Yes	11	7.1	144	92.9	
No. of outpatient physician visits					.21
Mean	6		6		
SD	4		4		
Screening mammography					.06
No	21	4.0	503	96.0	
Yes	273	6.1	4,234	93.9	
Disease stage and treatment					
Axillary lymph node involvement					.01
No	283	6.1	4,349	93.9	
Yes	11	2.8	388	97.2	
Metastatic disease					.61
No	287	5.9	4,584	94.1	
Yes	7	4.4	153	95.6	
Any axillary surgery					.01
No	43	4.1	1,002	96.0	
Yes	251	6.3	3,735	93.7	
Chemotherapy					.03
No	276	6.1	4,262	93.9	
Yes	18	3.7	475	96.4	
Endocrine therapy					.32
No	99	5.4	1,735	94.6	
Yes	195	6.1	3,002	93.9	
Health care access*					
Insurance type					.005
HMO	59	4.3	1,309	95.7	
Non-HMO	235	6.4	3,428	93.6	
Surgeon density*†					.24
Q1 (≤ 8)	79	6.3	1,182	93.7	
Q2 (9-11)	69	5.3	1,222	94.7	
Q3 (12-15)	60	5.0	1,136	95.0	
Q4 (> 15)	86	6.7	1,197	93.3	
Radiation oncologist density*†					.34
Q1 (≤ 8)	84	6.6	1,182	93.4	
Q2 (9-13)	71	5.8	1,146	94.2	
Q3 (14-19)	63	5.0	1,211	95.1	
Q4 (> 19)	76	6.0	1,198	94.0	

(continued on following page)

Table 3. Univariate Associations: Predictors of Use of Brachytherapy Alone Versus EBRT Alone in the Study Period From 2003 to 2006 (continued)

Variable	Brachytherapy Alone (n = 294)		EBRT Alone (n = 4,737)		P
	No. of Patients	%	No. of Patients	%	
Socioeconomic status*					
Metropolitan area					.50
No	28	5.1	520	94.9	
Yes	266	5.9	4,217	94.1	
Median income, $					.06
Q1 (≤ 40,305)	54	4.4	1,188	95.7	
Q2 (40,306-45,290)	80	6.4	1,175	93.6	
Q3 (45,291-52,936)	72	5.9	1,160	94.1	
Q4 (> 52,936)	88	6.7	1,214	93.2	
Percentage living in poverty					.25
Q1 (≤ 9.3)	83	6.4	1,216	93.6	
Q2 (9.4-11.8)	61	4.9	1,185	95.1	
Q3 (11.9-15.2)	85	6.5	1,216	93.5	
Q4 (> 15.2)	65	5.5	1,120	94.5	
Percentage with ≥ college education					.08
Q1 (≤ 17.2)	68	5.4	1,191	94.6	
Q2 (17.3-24.9)	56	4.7	1,128	95.3	
Q3 (25.0-29.5)	93	7.1	1,228	93.0	
Q4 (> 29.5)	77	6.1	1,190	93.9	

Abbreviations: EBRT, external-beam radiation therapy; SD, standard deviation; HMO, health maintenance organization; Q, quartile.
*By patient county of residence.
†Per 1000,000 persons.

thus conclusively demonstrate a local recurrence, breast cancer–specific survival, and overall survival benefit.[1,3]

Although initial studies of breast brachytherapy suggest reasonable short-term locoregional control rates (for example, a 3-year actuarial recurrence rate of 2% in the American Society of Breast Surgeons MammoSite Breast Brachytherapy Trial[7]), longer term results are highly anticipated, given the long natural history of breast cancer with an ongoing risk of recurrence even after several decades. Current published guidelines on the use of breast brachytherapy consider the limitations of available clinical data and are generally conservative in identifying patients at the lowest risk of recurrence as the most appropriate candidates for this therapy.[19-21] Consistent with guidelines, nearly all patients (94%) in our study treated with brachytherapy were free of axillary involvement or metastatic disease at the time of treatment, although future studies with explicit tumor staging information may seek to evaluate in more detail the frequency of guideline concordance. At the same time, less consistent with available data, our results demonstrated the dramatically increasing popularity of the balloon-based technique compared with the interstitial technique of catheter placement, ostensibly as a result of ease of balloon-based catheter placement. The majority of historical data on breast brachytherapy was based on studies using interstitial catheters, and only recently have larger patient cohorts been assembled to assess long-term efficacy of balloon-based techniques,[7] which may help to address the concern over potential differences in treatment volumes and dosimetry associated with the balloon-based system.

Nonclinical factors also played an important role in influencing the utilization of brachytherapy alone, with our results suggesting that the use of brachytherapy was nonuniform across patient subgroups and geographic regions. Neighborhood socioeconomic factors may have influenced patients' access or physicians' incentives to use this novel therapy. Various aspects of standard breast cancer treatment, including the receipt of chemotherapy, BCS, and radiotherapy after BCS, have been found to vary by sociodemographic variables, and in general, it has been reported that socioeconomic disadvantage is a barrier to appropriate receipt of standard therapy.[18,26-28] Our study is hypothesis generating, suggesting that factors associated with provider characteristics, provider-patient interaction, insurance environment, geographic practice patterns, and socioeconomic status[29-31] may also affect the diffusion of emerging treatments in breast cancer care. The significance of low density of radiation oncologists in predicting use of brachytherapy may suggest that the convenience factor associated with brachytherapy courses may indeed have affected decisions to implement this treatment option.[32] The significance of high density of surgeons in predicting brachytherapy may have further reflected patient access to new technology or may have potentially reflected provider behavior—for example, a response to competitive pressures or financial rewards in high-density markets or availability of collaborative knowledge and experience using new treatments associated with higher patient volumes. The associations with socioeconomic variables, which require further validation, could suggest a unique phenomenon of a reverse disparity, in which more advantaged, better insured patients would be more likely to receive a new, although nonstandard, treatment.

Our sample focused on older patients with breast cancer who were well insured with continuous Medicare plus private supplemental insurance coverage. Therefore, future studies will be required to validate the magnitude and significance of predictors of brachytherapy use among younger patients and patients with less comprehensive insurance coverage, in whom breast brachytherapy may have been

adopted less readily.[31] Because our definition of radiotherapy type was claims based, misclassification may have occurred. However, we chose to err on the side of increased specificity for the claim of brachytherapy versus EBRT, with patients who had nonspecific radiotherapy claims codes classified as receiving EBRT. Some patient, disease, and treatment details were unavailable in our claims-based database. Future studies may compare breast brachytherapy utilization with other partial-breast radiation treatment strategies (eg, three-dimensional conformal therapy). Additionally, future studies may focus on treatment adherence to other guideline criteria, such as younger age, tumor size, histology, multicentricity, and receptor status. Notably, the patient sample size (denominator) decreased in our analytic sample in the last two time periods. This potentially reflects the influence of the implementation of Medicare Part D on January 1, 2006. Residual confounding attributable to this factor may exist, and thus, future studies are particularly required to validate whether increased brachytherapy use during this time period existed in patients with various types of insurance coverage. Finally, additional studies are required to identify whether there were any underlying changes in patient, provider, or institutional factors during the study period that contributed to the apparent temporal and geographic variations in treatment utilization.

Despite ongoing questions regarding the long-term outcomes associated with breast brachytherapy and controversy over its routine use outside of the clinical trial setting, breast brachytherapy has been rapidly incorporated into treatment of older, well-insured patients with breast cancer in recent years, with the frequency of use as high as 10% in older insured patients. Our results suggest that the availability of clinical evidence demonstrating treatment efficacy is unlikely to have been the major force determining diffusion of this new technology. Instead, nonclinical factors, including policy and socioeconomic influences, seem to play an important role. In an era when new technologies and therapies are advancing rapidly yet, simultaneously, demands are growing to contain costs and establish treatment effectiveness, it is important to analyze available data to understand how decisions are made to use developing treatments such as breast brachytherapy. Insights gained may help to improve the rationale by which future therapies are promoted and adopted into care.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

Conception and design: Grace L. Smith, Ying Xu, Thomas A. Buchholz, Benjamin D. Smith, Sharon H. Giordano, Ya-Chen T. Shih
Provision of study materials or patients: Ya-Chen T. Shih
Collection and assembly of data: Ying Xu, Ya-Chen T. Shih
Data analysis and interpretation: Grace L. Smith, Ying Xu, Thomas A. Buchholz, Benjamin D. Smith, Sharon H. Giordano, Bruce G. Haffty, Frank A. Vicini, Julia R. White, Douglas W. Arthur, Jay R. Harris, Ya-Chen T. Shih
Manuscript writing: All authors
Final approval of manuscript: All authors

REFERENCES

1. Clarke M, Collins R, Darby S, et al: Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: An overview of the randomised trials. Lancet 366:2087-2106, 2005
2. Fisher B, Anderson S, Bryant J, et al: Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 347:1233-1241, 2002
3. Jatoi I, Proschan MA: Randomized trials of breast-conserving therapy versus mastectomy for primary breast cancer: A pooled analysis of updated results. Am J Clin Oncol 28:289-294, 2005
4. Veronesi U, Cascinelli N, Mariani L, et al: Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 347:1227-1232, 2002
5. McCormick B: Partial-breast radiation for early staged breast cancers: Hypothesis, existing data, and a planned phase III trial. J Natl Compr Canc Netw 3:301-307, 2005
6. Offersen BV, Overgaard M, Kroman N, et al: Accelerated partial breast irradiation as part of breast conserving therapy of early breast carcinoma: A systematic review. Radiother Oncol 90:1-13, 2009
7. Vicini F, Beitsch PD, Quiet CA, et al: Three-year analysis of treatment efficacy, cosmesis, and toxicity by the American Society of Breast Surgeons MammoSite Breast Brachytherapy Registry Trial in patients treated with accelerated partial breast irradiation (APBI). Cancer 112:758-766, 2008
8. Chen PY, Vicini FA, Benitez P, et al: Long-term cosmetic results and toxicity after accelerated partial-breast irradiation: A method of radiation delivery by interstitial brachytherapy for the treatment of early-stage breast carcinoma. Cancer 106:991-999, 2006
9. King TA, Bolton JS, Kuske RR, et al: Long-term results of wide-field brachytherapy as the sole method of radiation therapy after segmental mastectomy for T(is,1,2) breast cancer. Am J Surg 180:299-304, 2000
10. Krishnan L, Jewell WR, Tawfik OW, et al: Breast conservation therapy with tumor bed irradiation alone in a selected group of patients with stage I breast cancer. Breast J 7:91-96, 2001
11. Kuske RR, Winter K, Arthur DW, et al: Phase II trial of brachytherapy alone after lumpectomy for select breast cancer: Toxicity analysis of RTOG 95-17. Int J Radiat Oncol Biol Phys 65:45-51, 2006
12. Perera F, Yu E, Engel J, et al: Patterns of breast recurrence in a pilot study of brachytherapy confined to the lumpectomy site for early breast cancer with six years' minimum follow-up. Int J Radiat Oncol Biol Phys 57:1239-1246, 2003
13. Abelson R: Quickly vetted, treatment is offered to patients. The New York Times. http://www.nytimes.com/2008/10/27/health/policy/27device.html
14. Sher DJ, Wittenberg E, Suh WW, et al: Partial-breast irradiation versus whole-breast irradiation for early-stage breast cancer: A cost-effectiveness analysis. Int J Radiat Oncol Biol Phys 74:440-446, 2009
15. Thomson Healthcare: 2006 MarketScan Database Dictionary: Commercial Claims & Encounters, Medicare Supplemental & COB. Ann Arbor, MI, Thomson Healthcare, 2006
16. Nattinger AB, Laud PW, Bajorunaite R, et al: An algorithm for the use of Medicare claims data to identify women with incident breast cancer. Health Serv Res 39:1733-1749, 2004
17. Gold HT, Do HT: Evaluation of three algorithms to identify incident breast cancer in Medicare claims data. Health Serv Res 42:2056-2069, 2007
18. Smith GL, Shih YC, Xu Y, et al: Racial disparities in radiation therapy following breast conserving surgery: A national Medicare study. Cancer 116:734-741, 2010
19. American Society of Breast Surgeons: Consensus statement for accelerated partial breast irradiation. http://www.breastsurgeons.org/statements/APBI_statement_revised_100708.pdf
20. Keisch M, Arthur DW, Patel R, et al: American Brachytherapy Society, Breast Brachytherapy Task Group, 2007. http://www.americanbrachytherapy.org/resources/abs_breast_brachytherapy_taskgroup.pdf
21. Smith BD, Arthur DW, Buchholz TA, et al: Accelerated partial breast irradiation consensus statement from the American Society for Radiation Oncology (ASTRO). Int J Radiat Oncol Biol Phys 74:987-1001, 2009
22. Agresti A: Categorical Data Analysis. New York, NY, Wiley, 1990
23. Hosmer DW Jr, Lemeshow S: Applied Logistic Regression (ed 2). New York, NY, Wiley, 2000
24. Pawlik TM, Perry A, Strom EA, et al: Potential applicability of balloon catheter-based accelerated partial breast irradiation after conservative surgery for breast carcinoma. Cancer 100:490-498, 2004
25. Polgár C, Fodor J, Major T, et al: Breast-conserving treatment with partial or whole breast irradiation for low-risk invasive breast carcinoma:

5-year results of a randomized trial. Int J Radiat Oncol Biol Phys 69:694-702, 2007

26. Buchholz TA, Theriault RL, Niland JC, et al: The use of radiation as a component of breast conservation therapy in National Comprehensive Cancer Network Centers. J Clin Oncol 24:361-369, 2006

27. Chagpar AB, McMasters KM, Scoggins CR, et al: The use of radiation therapy after breast-conserving surgery in hormonally treated breast cancer patients is dependent on patient age, geographic region, and surgeon specialty. Am J Surg 195:793-798, 2008

28. Griggs JJ, Culakova E, Sorbero ME, et al: Effect of patient socioeconomic status and body mass index on the quality of breast cancer adjuvant chemotherapy. J Clin Oncol 25:277-284, 2007

29. Griliches Z: Technology, Education, and Productivity. London, United Kingdom, Basil Blackwell, 1988

30. Rogers EM: Diffusion of Innovations (ed 4). New York, NY, The Free Press, 1995

31. Shih YC, Elting LS, Halpern MT: Factors associated with immunotherapy use among newly diagnosed cancer patients. Med Care 47:948-958, 2009

32. Schroen AT, Brenin DR, Kelly MD, et al: Impact of patient distance to radiation therapy on mastectomy use in early-stage breast cancer patients. J Clin Oncol 23:7074-7080, 2005